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ORIGINAL ARTICLES

MEDICINE AND DUTY *

T. B. LAYTON, D.S.O., M.S. LOND.
SURGEON TO THE THROAT AND EAR DEPARTMENT OF GUY'S HOSPITAL; OTOLOGIST TO THE FEVER SERVICE OF THE L.C.C.

THE influence of Nelson's order of the day at Trafalgar has come down to us through more than a century. Its various manifestations affect our profession: there is the duty of the one and of the many; the duty of the immediate emergency and of the never-ending routine.

When a boy and a girl sign on at a medical school they join a profession in which they can no longer call any minute of their future lives their own. At any moment they may have to give up whatever they are doing to go and see someone in distress; that is one of the glories of our profession. If that distress is grave the doctor may have to collect a team to take action or to hand the patient over to a team which is in readiness. These are the aspects of duty in acute disease; and once one is inured it is not very hard to rise to them. It is no disparagement of the heroes of Trafalgar to say the same of their response to Nelson's signal, when everyone was on tip-toe for a fight. Far harder were the two years before Toulon when duty consisted in seeing that every day every rope and every spar was in its place, and when, for many, that was the whole of duty. In the same way we have with chronic disease a communal duty, made up of the personal duty of the many. Preventive and social medicine are developing around us. Our communal duty is not analogous to the work of a gun-team in the *Victory*, or even to that of her whole ship's company, but rather is comparable with the teamwork of the whole fleet. We have our firms at Guy's, the success of each depending on the sense of responsibility and duty of each member of it. But often one firm needs the assistance of another, and we have not yet replaced the enthusiastic emulation of competing firms by an equally enthusiastic fusion of firms working together. We must do this, and in such a way that for one patient a medical firm may fuse with an orthopædic firm, for another with an ear firm, while for a third all three or more may be needed; and we must see that the patient does not fall between two stools and that there is the same individual attention as there was when the patient was entirely under one man. Extend that idea to a similar fusion between different institutions, so that a patient may be at the same time under the care of someone at Guy's and someone else at an L.C.C. hospital nearby and perhaps under others at an L.C.C. hospital in the country or at Guy's-in-the-country, and under still more at a convalescent home or a rehabilitation centre belonging to a regional scheme. At present this idea that each of us should work for his patient in a medical world which includes several institutions is little developed; but we have to build a new code and a new etiquette between institutions.

DESTINY AND THE MIDDLE EAR

I want to try to illustrate these considerations by discussing the inflammations of the middle-ear cleft which I believe form today our most important medical problem from the national point of view. I know that I am suspect in making such a statement, for they have been my daily task between the wars. First there are cases of acute inflammation of the previously undamaged middle-ear cleft, most of which get well by the processes of nature. But a small number demand immediate action by the emergency team and are just as urgent as the most fulminating form of appendicitis; and as with appendicitis the final decision depends on the correct appreciation of a single physical sign. Rigidity of the neck is to otitic meningitis of acute disease what rigidity in the abdomen is to commencing peritonitis; and this neck-rigidity may be as difficult to assess as that in the right iliac fossa. One thing is certain: when you see a discharging ear and a suspicion of rigidity of the neck it is your duty to see that, to quote Wilfred Trotter, "the patient should at the earliest possible moment be put in conditions where any operation that may become necessary can be most safely and quickly performed."

The death of a child is a tragedy; but from the national standpoint it is not merely the fact of death that matters, but the influence which this has on the lives of others. When a father or a mother dies and leaves children destitute, the results are more far-reaching than when one of the children is taken away; and this is what happens when an intracranial complication of chronic ear disease arises, for they arise in middle age. Every one of these cases is a drama; sometimes it has a happy ending and then we keep in touch with the patient for several years, greeting him with pride, knowing he would not be there if it had not been for us. Sometimes it is a tragedy and our part ends in the post-mortem room, examining the intracranial contents to see what we can do in the next case to ensure that it may take a different course. The tension of a week's wasted work dies down and leaves us in that state of mental collapse which leads us to push the whole matter out of our minds. But it is only the end of the third act of tragedy for the family, left either without its wage-earner or without the mother. We all hope to start our children in life where we left off; we are beginning to wonder whether this is a wise wish, but there it is. With the extinction of the wage-earner that hope is gone. The mother has to take his place and the general standard of living goes down, in many instances, to one in which nutrition and even decency are impaired. When the mother dies it is worse; the loss of that life takes effect unto the third and fourth generation. These cases put the inflammation of the middle-ear cleft in the forefront of medical problems of national importance, because they are a group of tragedies which could have been prevented—and which should be prevented in the future.

Other results affecting the national weal follow failure to cure an acute inflammation of the middle-ear cleft. An infant begins to learn by the sense of feel; then the sense of sight is brought into play. When he learns to walk he passes out of infancy, and education may be said to begin. In the early stages of education hearing is the master sense; he needs it to learn to speak and to pick up scraps of knowledge from those around. I do not think that the importance of this stage of a child's education is sufficiently realised. If there has been some hardness of hearing he may be so backward as to lead to a suspicion of mental deficiency. One of the most difficult examinations in clinical medicine is to test the hearing at this age and to decide whether there is any deafness; but I consider that hardness of hearing which we can hardly call deafness is of serious consequence to the developing mind up to the age when a child can read, and read freely. Thus every acute inflammation of the middle-ear cleft if it is not cured before it changes to chronic disease or before there is permanent damage to the middle ear, may alter the whole of the patient's life.

An elaborate organisation has been set up by the Board of Education over the whole country, under the Children's Act of 1906, to deal with chronic ear disease in children of school age. Doctors, nurses, teachers, and many other people have given their attention to this work; and nothing has come of it in thirty years. That is what we have to face: chronic ear disease is incurable. It can be prevented by curing the preceding acute inflammation; but once the cutaneous or other secondary organisms have become established the disease is in most cases incurable. Many will say I am wrong. But though they may have helped many cases of chronic otitis media to get well, these are very few compared with the number of the population going about with chronic ear disease. We must approach the problem from a new aspect. Let us consider how chronic ear disease affects life after the school age has been reached. We may divide it into the effect on education and the effect on the wage-earning capacity. For the seriously deaf child there are special schools with expert teachers, or arrangements are made for the child to sit in front of the class near the teacher. But these form but a small part of the problem. It is the children with an unassessable diminution of hearing, or with deafness

* A lecture given on the eve of Trafalgar day, 1941, at Guy's Hospital.

not serious enough to warrant special arrangements, that waste the nation's energy, because they are not gaining as much from their education as they should. They go out into the world less expert than they should be, whatever their work, because their mental processes are not developed as much as they might have been.

The effect on wage-earning capacity is more uncertain. I do not believe that mere discharge from an ear ever results in a person losing work, having to take work of a lower standard, or having to go off duty. Once the patient has learned how to make a proper toilet of the meatus none of these things will happen: the only reason for his drawing sickness benefit is his doctor's suggestion that he should. There is no reason why anyone should stop work or be admitted to hospital on account of ear discharge without any other symptom. With deafness the problem is more intricate. Once a person is in work he does not lose work because of it. But a deaf man finds great difficulty in getting posts and in holding them; and he is often driven to do poorly paid menial work below the level for which his mental faculties qualify him. But the process does not necessarily end there; he may be driven down into the ranks of the unemployed, from whom come the unemployable. This national problem will in the future become more important because the effect of deafness, or even of hardness of hearing, is much greater in the woman than in the man. There are many jobs a man can continue to do with little or no hearing, but very few in which a woman can retain her post.

We must look, then, on every case of acute inflammation of the middle-ear cleft that becomes chronic as a failure, not for any given doctor but for the medical profession as a whole. It is not a matter for specialists, it is one of those bits of medicine common to the whole profession. We must all try to realise that if we have under us a patient with an acute inflammation of the middle-ear cleft we have a short six weeks in which to get it well from the date on which the drum-head ruptures; and by well I mean with a healed drum and normal hearing. We must use that combination of preventive and social clinical medicine of which I spoke earlier, and it will need the teamwork of the whole fleet. But no-one will see the results of his own work; what we do today will take effect in A.D. 2000.

EPIDEMIC NEONATAL DIARRHŒA IN MATERNITY HOSPITALS

I.—CLINICAL ASPECT

GEORGE ORMISTON, M.D. EDIN., M.R.C.P.E.

(*Working for the Medical Research Council, London*)

SERIOUS outbreaks of diarrhœa among babies in maternity hospitals have been described of recent years. Excellent accounts of their epidemiological and clinical features have appeared in America (Barenberg et al. 1937,* Frant and Abramson 1937, Rice et al. 1937, Best 1938), where attention has been drawn to their widespread distribution, high morbidity and mortality, and unexplained ætiology. Apart, however, from a paper by Craig (1936) little has appeared to indicate the prevalence of neonatal disease of an epidemic character in this country. The purpose of this communication is to summarise the results of studies into the nature of three of these outbreaks in different cities in England during the latter half of 1940.

These epidemics, which are sometimes referred to as epidemic diarrhœa of the newborn, are probably more common than is generally realised. Because of their tendency to high morbidity and mortality it is important that their features should be recognised as early as possible. We hope that the present account will lead to their more frequent recognition.

The cause or causes of diarrhœa in the neonatal period have not been satisfactorily established, and the opportunity has been taken to pursue certain bacteriological investigations which will be described in a later section of this paper. The outbreaks will be labelled respectively A, B and C. A and B affected hospitals in widely separated cities in the south of England, and C a hospital in a large city in the industrial north.

* References will be found at the end of the second paper.

OUTBREAK A

This occurred in a voluntary lying-in hospital of between 50 and 60 beds. The building is comparatively old and has 5 public wards and 7 small private rooms. There are 10 beds and 10 cots to a ward. There is a single labour room situated between the babies' bathroom and a distributing kitchen. The babies are washed, changed and fed (if not on the breast) in the bathroom. This leads to much contact between them. The hospital is understaffed. There is no division of duties, so that the same nurse attends the mother and feeds, changes and washes the infant. Breast-feeding is the rule, but, when cow's milk is necessary, a pasteurised product is used, suitably diluted, and acidified with lactic acid. It is stored in a refrigerator in a special milk room. Glucose water is given to all babies.

The first baby became ill on May 10, 1940, with sudden loss of weight, severe diarrhœa and some vomiting, and exhibited other symptoms such as drowsiness, dehydration, elevated temperature, a toxic appearance and a hoarse cry. Thenceforth, cases of varying severity appeared every few days through June into July. All the wards and all the babies in the private rooms were affected, and though measures were taken to check it the outbreak persisted until the hospital was closed to further admissions.

Period of epidemic prevalence (May 2–July 20, 1940)	
Babies born during this period	250
Babies who exhibited symptoms in hospital .. (10 came under our observation.)	27
Deaths from neonatal diarrhœa in hospital .. (Deaths at home are not accounted for.)	5

OUTBREAK B

This concerned the maternity department of a municipal hospital serving a large city about 130 miles from A. The department is of modern construction, and was opened in 1939. It consists of two identical one-storied buildings separated by a grass plot and with no indoor communication. Each comprises two wings joined together in a wide V facing roughly south. Each wing is subdivided into 11 single or double rooms and 2 small wards of 3 beds. The total number of beds in the department amounts to 88.

By contrast with A, the babies sleep together in a large central nursery, and here they are changed and fed if not on the breast. A bathroom and an isolation room adjoin the nursery. Cots are placed side by side on the framework of a movable trolley which is wheeled along the passage to the respective rooms at feeding time. The artificial foods in use include pasteurised milk, Nestlé's, Trufood and Allenbury's. These are kept in the cupboard of a kitchen used for food distribution to the mothers, and there is no refrigerator. Glucose water is given to all babies. Here again the nurses share the duties of attending to mother and child. Each wing has its own labour-room and a separate personnel. A swing door in the passage between the wings can be closed to ensure the mechanical isolation of one wing from another.

When the outbreak came under our notice it appeared to be confined to one wing, where the first diagnosed case occurred on July 7, 1940, and the last on July 27. Out of 42 babies exposed, 14 became ill in hospital at intervals of a day or two; a follow-up inquiry revealed that an additional 12 babies developed the disease within a few days of reaching home and must have been discharged during the period of incubation.

Months later unmistakable cases were recognised in both wings of the twin block. The evidence suggests that the outbreak really began about the middle of June and ran without intermission in one wing or another until it was checked in December. Many deaths occurred, and though all the cases had pronounced gastro-intestinal symptoms, the stated cause of death was rarely connected with or attributed to them. The closing of a block about the third week of November appears to have stopped the outbreak.

Period of epidemic prevalence (June 17–Dec. 15, 1940)	
Babies born during this period	540
Minimum number of babies affected in hospital (25 came under our observation.)	83
Deaths from neonatal diarrhœa in hospital ..	25

OUTBREAK C

This outbreak took place in the modern section of an older hospital serving a large industrial population. Unfortunately we did not hear about it until it was over, so that there was no opportunity of studying it at first hand. The maternity unit comprises 4 wards of 6–12 beds each, and 5 single or double rooms, distributed on two floors. The ground floor has its own labour-room, and in addition an isolation unit and nursery. The first floor takes the larger number of patients, has 2 labour-rooms, an operating-theatre and 2 nurseries, one of them for premature babies. The total number of beds is 43.

Between July 2 and Sept. 29, 1940, 29 babies became ill in hospital, most of them in July and August. Many of the cases were severe, and the fatality (38%) was the highest of this series. The characters of the epidemic were similar to those already described. One main difference in the regimen of this hospital as compared with the others is the preponderance in the use of cow's milk.

Period of epidemic prevalence (July 2–Sept. 29, 1940)	
Babies born in hospital during this period ..	206
Babies affected in hospital	29
Deaths from neonatal diarrhœa in hospital ..	11

EPIDEMIOLOGY AND ÆTIOLOGY

Further experience must be gained before adequate discussion under this heading is possible. Each of the three epidemics started explosively, so that considerable numbers of infants were affected within a week or two; after this they progressed more slowly, outbreaks A and B continuing for weeks or months till the hospital was closed. Whatever the causal agent, and by whatever mechanism fresh cases are promoted, it can be said that, once the trouble starts, known methods of isolation as practised do not seem capable of stopping it, and that the individual cases are mild, moderate or severe without reference to such factors as sex, birth-weight, age at onset or stage of the epidemic.

Season.—The outbreaks all began in the warm summer months. It is reported that epidemics may occur at any season. All that can be said is that outbreak B continued without remission through summer into winter (December).

Incubation period.—Certain criteria from A suggest that this is short—from 1 to 8 days.

Age-incidence.—Most babies in outbreaks A and B became ill within the first week of life—the great majority within a fortnight. However, the youngest infants are not alone susceptible, as a follow-up (part of B) revealed that many babies developed diarrhœa after being discharged from hospital apparently well. Again, in C, where for various causes numbers of infants were kept in hospital longer than the usual 10–14-day period after birth, 46% were older than a fortnight when first affected.

Causal origin.—In view of the early age (4 days) at which signs may appear, and the short incubation period, the possibility must be envisaged that the disease is congenital or at least transmitted from mother to child at, or immediately after, birth. In fact, the mothers were healthy for the most part and delivered of apparently healthy children, and where there was maternal illness (eclampsia, pyelitis, breast abscess) it seemed to be no more prevalent among the mothers of affected than among those of the unaffected children. No evidence was discovered to implicate as causal factors morbid conditions such as colds, influenza, furuncles or digestive disturbances among the medical or other staff. Many babies both ill and well had a mild conjunctivitis (? prophylactic use of silver nitrate). A few had minor sepsis of the umbilicus or subcutaneous abscesses. Preceding infections of the upper and lower respiratory tracts, or of the central nervous system, were not found. Terminal bronchopneumonia was noted in some and discovered in others at autopsy, as was also pus in the middle ear.

Routine bacteriological throat and stool cultures were obtained from babies, mothers, medical and domestic staff in outbreaks A and B, and stool cultures from the babies in C, but none of the usual pathogens was found. Cultures from pus in the middle ear revealed organisms of the coliform and diphtheroid groups, as well as occasional staphylococci and streptococci.

Morbid anatomy.—Careful autopsies were performed on 9 subjects, 1 in outbreak A and 8 in B. None showed changes of note. As a rule the intestinal tract was normal anatomically and histologically. In one or two cases the intestinal mucosa was slightly hyperæmic. The liver, adrenals, spleen, kidneys and central nervous system were little, if any, different from the normal. The presence of terminal bronchopneumonia and otitis media in some instances has been remarked on.

ONSET AND COURSE OF DISEASE

The onset may be sudden or insidious. All three epidemics included examples of both. In B, many of the cases began slowly and appeared to be difficult to recognise in the early stages. In cases of insidious onset the baby begins to suck less vigorously, or becomes indifferent to food, appears slightly limp and ceases to put on weight. These signs are often misinterpreted. The breast milk is thought to be insufficient and a complement of cow's or other milk prescribed. Again, the disease may begin with a mild diarrhœa or merely a green stool, or there may be slight vomiting or a definite loss of weight.

The sudden onset is characterised by profuse diarrhœa, and usually vomiting, and sometimes a dramatic loss in weight. Where the onset is early (4th or 5th day) the physiological drop in weight is at its maximum, or a gain in weight may have set in. A failure to gain, or a further dramatic drop, may be the first sign that the infant is affected. In outbreak C a few infants in the premature class simply showed signs of collapse with anorexia and a greyish or cyanosed appearance, and died in a day or two without diarrhœa or vomiting. This type of onset has also been noted in some aged victims of true dysentery.

In the milder type of case, the stools become rather frequent, 2–5 daily, relaxed or slightly loose, green or yellow in colour. The appetite is as a rule indifferent but may be quite good, and an alteration in the colour of the stools for several days on end may be the only sign of abnormality. Constitutional symptoms are barely discernible. There is no dehydration, no rise in temperature, and beyond a faint pallor and a failure to gain in weight progress seems satisfactory. The stools may become normal and the whole process be over in a few days. But relaxation of the stools may persist for a week or two, and though there may be a continued absence of the more serious symptoms the appetite will remain poor, and the return to birth weight will be considerably delayed.

In those moderately ill, the stools are more frequent—up to 7 or more in the 24 hours. They are apt to be loose or watery, bright green, or yellow or orange. The infant may vomit once a day or more often. The weight falls by 8–16 oz. within 3–4 days of the onset. The baby becomes listless or drowsy and feeds slowly and reluctantly, has a pale or greyish appearance, and may or may not be manifestly dehydrated. He looks somewhat toxic, and the temperature is unstable—rising or falling a degree or so above normal. The illness lasts at least a week, and is generally prolonged into the second or third week, when recovery sets in with improvement of the appetite and a slow but steady accretion of weight. The stools return to normal rather slowly, and tend to remain a little relaxed or green while the infant is much better in all other respects.

The really serious cases are unmistakable. They become worse rapidly with diarrhœa and vomiting and sudden loss in weight. Vomiting is usually serious, frequent, sometimes projectile, and occurs after food and fluid. It may precede the onset of diarrhœa by a day or two and there is often a degree of abdominal distension. The stools number 3–10 in the 24 hours, are loose or watery, and are apt to vary in colour from time to time, from green of different hues to yellow or brown, and, characteristically, orange. Colic is not a feature. The loss of weight is considerable—1–2 lb. for the average baby. There is serious dehydration, drowsiness alternating with irritability, and sometimes a degree of neck rigidity; but the fontanelle is sunken, and an examination of the cerebrospinal fluid will reveal no change. The face becomes ashen grey, the eyes sunken, and at intervals the lips may be cyanotic. The temperature hovers around 100° F., but may reach 103° F. or 104° F., and the infant looks profoundly toxic. Death usually

occurs within ten days, sometimes sooner, and generally within a fortnight. Alternatively the symptoms may abate and slow recovery set in.

So far as our limited observations go, complications do not appear to be common. Otitis media is seldom obtrusive, but too few autopsies were undertaken to enable us to judge its real incidence. The same may be said of bronchopneumonia, which when it occurred generally appeared in the final stages of the illness.

PROGNOSIS AND TREATMENT

The prognosis is good in mild and moderate cases, and bad in those defined as serious. Of those considered serious 62% in outbreak A and 81% in B died. The onset of frankly fluid stools, repeated vomiting, restlessness and a hoarse cry worsen the prognosis. The colour of the stools means little. Orange stools may be present in mild cases as in serious. The type of feeding may have some influence on the outcome. In outbreak B, 14% of 51 sick infants entirely breast fed died, contrasted with 60% of 30 given artificial milks with or without breast milk. In outbreak C, all the infants were being fed on cow's milk mixtures when they developed the disease, and the case-fatality was 38%.

No treatment is specific. In all but the mildest, parenteral administration of nutrient and salt-replacement fluids, and of blood or plasma is necessary. In outbreak C, sulphapyridine was tried in some cases without success. Sulphathiazole was tried in those instances where staphylococci were isolated from the stools. The presence of these organisms is of problematical significance, so far as our investigations go, and the drug appeared of little value. Breast milk would seem to be the feeding of choice.

There is only one effective means of halting the spread of the epidemic, and that is to close the entire hospital to admissions, discharge the patients, and thoroughly clean and disinfect the wards before reopening in a week or ten days' time.

COMMENT

Neonatal diarhœa of an epidemic character has recently been described by Rice and his colleagues (1937) as a disease sui generis, using such criteria as (1) its apparent limitation to babies in the first month of life to the exclusion of older infants; (2) the apparent absence of parenteral disease to which it might be secondary; and (3) its non-identification with any known enteral disease. However, during infancy the syndrome of diarrhœa, vomiting and associated effects identical with that of neonatal diarrhœa may arise from a number of infections well recognised or obscure, and until it has been established that epidemics of diarrhœa among the newborn are due to one and not to various ætiological agents the basis for regarding them as specific must rest on an insecure foundation.

Meantime, the term "epidemic diarrhœa of the newborn" will serve a useful purpose if it leads to the more critical scrutiny of infants during their sojourn in hospital, and to the recognition of diarrhœa of an epidemic character at an early stage. Mild cases are easily missed. Slight loss of weight or vomiting in very young infants is a customary experience from irrelevant causes, and apt to be regarded casually by nurses and even experienced sisters. The occasional green stool is a commonplace, and it is unnecessary to exaggerate the importance of these minor symptoms. But it should be borne in mind that for a period of weeks they may be the only token that one baby after another is being affected by the disease in question, until there is a sudden flare-up of serious cases, some of which will be fatal. Another danger is that a considerable proportion of babies may be discharged apparently well but incubating the disease. They are lost sight of. Many of them will be admitted to children's hospitals, where the origin of the disease is never suspected. In fact the number affected by epidemic diarrhœa and the total mortality is probably much greater than one may conclude from a mere study of maternity hospital statistics.

Epidemic diarrhœa of the newborn is not a new disease. It has probably occurred as long as maternity hospitals have been in existence. But the gravity of its effects have not been sufficiently realised. The repetition of an outbreak in the same institution does not appear to be common until, perhaps, after the lapse of many years, so that hospital staffs are not familiar with it, and may not tackle it boldly at the beginning.

Furthermore we have the impression that where an outbreak does arise the hospital authorities tend to be unduly reticent, fearing perhaps for the reputation of the place. Until we are able to prevent these outbreaks it is probable that they will become more common with the expansion of hospital facilities and the decreasing number of confinements in the home. If what has been described in these three epidemics reflects, as it may well do, a state of affairs occurring in other large centres of population, the total of wasted life and effort must be already considerable, and one that the nation cannot afford, least of all now.

When an outbreak is suspected no effort should be spared to determine its true nature, and until this has been done rigid methods should be employed to safeguard those as yet unaffected. When a definite diagnosis has been reached the hospital should be closed at once and the patients discharged. If, at the same time, a careful investigation could be made and the results brought to the notice of the profession the accumulated data would add to our knowledge and might aid in the solution of the problem.

SUMMARY

Three outbreaks of diarrhœa confined to newborn babies arose during the latter half of 1940 in maternity hospitals serving three widely separated cities in England. They were essentially similar in their epidemiological and clinical features. Large numbers of infants were affected and there was an aggregate case-fatality of 29%.

It is suggested that outbreaks of neonatal diarrhœa are of more general occurrence than is realised, and may constitute an important factor in the maintenance of high neonatal mortalities.

It is important that the nature of these outbreaks should be recognised at an early stage so that measures can be taken for the safety of present, and the prevention of future, contacts.

EPIDEMIC NEONATAL DIARRHŒA IN MATERNITY HOSPITALS

II.—BACTERIOLOGICAL ASPECT

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HITHERTO the bacteriological findings in neonatal diarrhœa, or epidémic diarrhœa of the newborn as it is often called, have been variable and inconclusive. In the United States McKinlay (1937) isolated an unidentified species of salmonella from the stools. Kimberley (1939) found *Clostridium welchii* to be the predominating organism in the stools, but he did not regard it as of any ætiological significance. Costello and Lind (1939) attributed the disease to a pathogenic strain of *Proteus vulgaris* associated with *Bacterium coli*. Cron, Shutter and Lahmann (1940) cultured hæmolytic streptococci from the throat and from the stools of all the cases examined, and from the peritoneal fluid in 10 out of 13 cases coming to autopsy. Frant and Abramson (1938), Greenberg and Wronker (1938), and Forbes and Olsen (1939), on the other hand, failed to find any bacteria of importance. In this country Bloch (1941) states that in the outbreak he studied infection was obviously respiratory, and that staphylococci were found in the nose of some of the cases and contacts.

In starting our inquiry it seemed important (*a*) to make as complete a study as possible of the bacterial flora of the fæces of normal and affected infants, and to find out whether the qualitative or quantitative distribution of organisms in the stools was disturbed during the course of the disease; (*b*) to search for known pathogenic organisms, such as those of the salmonella and dysentery groups; and (*c*) on the analogy of lamb dysentery to determine whether toxins formed by anaerobic

spore-bearing bacteria or by other organisms were present in the fæces. With these objects in view a fairly elaborate technique was designed of which the following is a summary.

TECHNIQUE

A film of the fæces was stained by Gram's method and examined to see if there was any obvious abnormality in the relative numbers of bacterial types present.

Search for organisms of the salmonella and dysentery groups was made by direct plating on MacConkey's agar, and for organisms of the salmonella group in addition by preliminary enrichment in brilliant green and tetrathionate broths.

A suspension of fæces was made in N/4 Ringer solution, standardised by opacity to 3000 million coliform bacilli per ml., and treated as follows. (*a*) One part was heated to 70° C. for 10 minutes and plated out in duplicate on a glucose blood agar medium. One plate was incubated aerobically and the other anaerobically to detect spore-bearing organisms. (*b*) The other part was not heated. Instead, successive tenfold dilutions were made in N/4 Ringer, and 0·1 ml. quantities of the 10^{-2}, 10^{-3}, 10^{-4}, and 10^{-5} dilutions were spread on plates of dry blood agar, glucose blood agar (Eggerth and Gagnon 1933), or liver glucose blood agar (Eggerth 1935), which were incubated anaerobically in a modified McIntosh and Fildes jar and examined usually after 48–72 hours and then again after four or five days. These plates were used for determining the relative numbers and types of micro-organisms present. The identification of the different types was carried out by the usual routine methods. Preliminary observations failed to reveal any advantage in the incubation of plates aerobically as well as anaerobically, and aerobic incubation was therefore discontinued.

The standard suspension was centrifuged at high speed, and tested for toxicity by the inoculation of 0·1–0·2 ml. of the supernatant fluid intravenously into mice, and sometimes intraperitoneally as well.

The fæces were usually examined on the same day as that on which they were passed. If they arrived too late to be examined the same day, they were kept in the refrigerator overnight. In some instances they were transmitted by post or rail and did not arrive till the following day. Experimental observations on healthy infant stools subjected to these different methods of storage showed that little change in the normal flora resulted. Fæces from sick babies were often inoculated immediately after collection on to MacConkey agar plates, in case dysentery bacilli should be present and die out during transmission to the laboratory.

FINDINGS IN NORMAL NON-CONTACT INFANTS

At Oxford specimens of stools from 21 healthy non-contact infants aged 7–23 days were examined, and at Cambridge from 36 healthy non-contact infants aged 3–16 days. These infants were all in maternity homes free from neonatal diarrhœa. All infants were breast fed, though complementary feeds of modified cow's milk were given to a few of them. The results are recorded in table I. The figures on the whole agree very closely. Oxford recorded a slightly higher proportion of coliform bacilli and Cambridge a slightly higher proportion of lactobacilli, but in view of the great variation in frequency to which all groups of organisms were subject in fæces from different infants no weight can be attributed to this discrepancy. It will be seen that about 80% of the organisms cultured from the fæces belonged to the lactobacillus group, about 10% to the group of coliform bacilli, and about 4% each were streptococci and staphylococci. Organisms of the Gram-negative bacteroides group (Eggerth and Gagnon 1933, Weiss and Rettger 1937, Misra 1938) and of the clostridium group were rarely present.

Examination of the individual strains showed that practically all of the lactobacilli were of the *bifidus* type. Most of the coliform bacilli were *Bact. coli* I type (Report 1939), though occasional strains were identified as *Bact. aerogenes*, or belonged to the late-lactose-fermenting or paracolon groups. Proteus seemed to be very uncommon. Of the streptococci present only a proportion were studied fully. The great majority of these corresponded to *Streptococcus fæcalis*, being heat-resistant diplococci, fermenting mannitol but not raffinose, producing the characteristic acid clot with decolorisation in litmus milk, and falling into Lancefield's group D. A few of the strains produced true β-hæmolysis, but most were α-hæmolytic. With one exception the staphylococci were of the *albus* type and were coagulase-negative. *Staphylococcus aureus* was never found in stools from healthy infants at Oxford, and only once at Cambridge. The very few anaerobic spore-bearers that were isolated seemed to be closely related to, if not identical with, *Cl. paraputrificum*, Bienstock (Hall and Snyder 1934).

These findings are in general accord with the classical observations of Tissier (1900), who first drew attention to the great predominance of *Lactobacillus bifidus* in the stools of healthy breast-fed infants.

The intravenous inoculation of mice failed to reveal the presence of any soluble toxin in the stools. At Oxford the animals remained alive and well till they were killed on the fifth day or later. At necropsy nothing abnormal was found. At Cambridge the animals were kept under observation for a longer time. Most of them died in 10–35 days after injection. No obvious changes were seen post mortem, but from the heart blood or peritoneal cavity coliform bacilli were cultivated. These results were attributed to chronic infection with organisms present in the supernatant fluid of the fæces suspensions.

FINDINGS IN OUTBREAK A

Samples of stools from 18 *normal contact* infants aged 1–22 days were examined at Cambridge with the results shown in table II. Compared with the findings in normal non-contact infants at Cambridge (table I) considerable differences are noticeable. The lactobacilli constitute only a small proportion of the fæcal flora, while the coliform bacteria and the staphylococci are preponderant. Too much attention should not be paid to these differences, since owing to the large number of specimens received at once the full quantitative technique could not be carried out, and the figures are therefore open to criticism.

Samples of stools from 9 sick babies suffering from diarrhœa were examined at Cambridge and 3 at Oxford. Macroscopically the stools did not differ greatly from those of the healthy controls. Mucus was not infrequently present in small quantity, but not more often than in the stools of the control babies. Pus or blood was never observed. With few exceptions the reaction was acid to litmus. The bacteriological findings are summarised in table II. Compared with the figures for normal contact infants in the same hospital, the lactobacilli are seen to be more numerous and the staphylococci less numerous. The figures for the coliform bacilli and for the streptococci are much the same. In 6 cases the stools were examined after recovery; the results were not appreciably different from those in the early stage of the disease.

The number of samples examined in this outbreak was relatively small and the observations on the control normal contact infants were not altogether satisfactory. There does not appear, however, to be any considerable difference in the bacterial flora of the stools from the sick and healthy infants in the same hospital, and certainly none that would suggest an adequate cause for the occurrence of diarrhœa.

No organisms of the salmonella or dysentery groups were isolated from any of the stools, and in none of them was a soluble toxin demonstrated by mouse inoculation.

FINDINGS IN OUTBREAK B

Samples of fæces from 14 normal contact infants were examined at Oxford and 10 at Cambridge. The results are given in table III. The Cambridge figures showed a lower proportion of lactobacilli and of coliform bacilli and a higher proportion of streptococci than the Oxford figures. Taken together it will be seen that the chief difference in the distribution of organisms from that in healthy non-contact infants at Oxford and Cambridge (table I) is that the lactobacilli, though still dominant, are less numerous, and the coliform bacilli, and particularly the streptococci, are more numerous.

From sick infants suffering from diarrhœa Oxford examined 10 stools and Cambridge 12. Macroscopically most of the stools were similar to those of healthy babies on a milk diet. Mucus was not infrequently present in small quantity, as it was in the stools of the control contact infants, but pus and blood were absent. With few exceptions the reaction was acid to litmus. The bacteriological findings are summarised in table IV. At Oxford a higher proportion of lactobacilli and a lower

TABLE I—DISTRIBUTION OF BACTERIA IN FÆCES OF NORMAL NON-CONTACT INFANTS AGED 3–23 DAYS

Type	Oxford (21 infants)			Cambridge (36 infants)			Oxford and Cambridge (57 infants)		
	Samples positive	Per cent. of flora		Samples positive	Per cent. of flora		Samples positive	Per cent. of flora	
		Limits when present	A.M.		Limits when present	A.M.		Limits when present	A.M.
Lacto-bacilli	21	1–100	75	35	29–99	84	57	1–100	81
Coliform	18	<1–99	16	32	<1–60	7	50	<1–99	10
Strepto-cocci	8	<1–49	5	14	<1–46	3	22	<1–49	4
Staphylo-cocci	7	2–20	3	25	<1–49	4	32	<1–49	4
Bacteroides	1	17	1	—	—	—	1	17	<1
Clostridia	1	<1	<1	11	<1–4	2	12	<1–4	1

Fæces at Oxford were plated on liver blood glucose agar, at Cambridge on blood agar or glucose blood agar.
A.M. = arithmetic mean.

proportion of coliform bacilli were found than at Cambridge; otherwise the results agree fairly closely. Compared with the findings from the control contact infants in institution B (table III), the combined figures for the sick infants show a higher proportion of coliform bacilli and a lower proportion of streptococci.

From no sample of fæces were salmonella or dysentery bacilli isolated, and no sample was found to be toxic for mice.

Since it seemed possible that neonatal diarrhœa might be due to a staphylococcal enterotoxin elaborated in the maternal breast, an examination was made for staphylococci in the milk of sick babies' mothers. Ten strains of these organisms were isolated from seven samples of milk. Four of them proved to be of the *aureus* and six of the *albus* type. The four *aureus* strains were coagulase-positive and three of them produced an α-hæmolysin. None of them produced a β-hæmolysin, and none of them produced enterotoxin as judged by the kitten test of Dolman, Wilson and Cockcroft (1936). The six *albus* strains were all coagulase-negative, hæmolysin-negative and enterotoxin-negative.

Five strains of staphylococci were isolated at Oxford from the fæces of infants with neonatal diarrhœa. Two of these were of the *aureus* type, and were coagulase-positive but enterotoxin-negative. Three were of the *albus* type and were both coagulase- and enterotoxin-negative.

FINDINGS IN OUTBREAK C

No samples of fæces were available from this outbreak, but six strains of staphylococci that had been isolated from the milk of a tuberculin-tested herd supplying the hospital were sent for examination. Four of the strains were of the *aureus* type. They were coagulase-positive, and produced an α-hæmolysin and an enterotoxin. The enterotoxin formed by two of the strains was so powerful that the kittens died within 24 hours. Only one strain was tested for β-hæmolysin, and this was positive. Of the two other strains, one was of the *albus* type and the other produced an orange pigment. Both were coagulase- and enterotoxin-negative.

TABLE II—OUTBREAK A: DISTRIBUTION OF BACTERIA IN FÆCES OF 18 NORMAL CONTACT INFANTS AGED 1–22 DAYS, AND OF 12 SICK INFANTS AGED 4–21 DAYS

NORMAL CONTACT INFANTS				SICK INFANTS			
Type	Samples positive	Per cent. of flora		Type	Samples positive	Per cent. of flora	
		Limits when present	A.M.			Limits when present	A.M.
Lactobacilli	11	2–41	11	Lactobacilli	10	2–73	30
Coliform	17	<1–96	44	Coliform	12	8–96	55
Streptococci	5	<1–91	6	Streptococci	12	1–21	8
Staphylococci	14	1–90	32	Staphylococci	7	<1–15	4
Other organisms *	11	1–64	7	Bacteroides	1	45	4
				Clostridia	2	<1	<1

* Other organisms comprised mainly micrococci and diphtheroids.

DISCUSSION

The main question at issue is: What is the cause of neonatal diarrhœa? The following possibilities must be considered.

(1) *Specific infection with an organism of the salmonella or dysentery groups.*—Though Hormaeche and his associates (Bonaba et al. 1940) found that 20% of enteritis in infancy and childhood in Uruguay were due to salmonella infection, and 32% to dysentery infection, we have completely failed to isolate any member of these groups of organisms. It may be remarked that so far as we are aware Hormaeche did not examine any outbreak of neonatal diarrhœa. With the exception of a single outbreak described by McKinlay (1937), who reported the isolation of an unidentified strain of salmonella from the stools of the infants during life and from the heart blood and viscera of one case at autopsy, no evidence has yet been adduced to incriminate these organisms in the causation of this condition.

(2) *Infection with a normally non-pathogenic bacterium.*—This is the view taken by Costello and Lind (1939), who attribute the disease to a pathogenic strain of *P. vulgaris* associated with *Bact. coli*. Cass (1941) likewise seems to take the same view. She found an organism, which was identified, probably incorrectly, as *B. lactis aerogenes*, in the fæces of 5 sick infants. From 2 of the infants that died it was isolated from a consolidated lung and from an umbilical thrombus respectively. Since, however, the same organism was found in the fæces of at least 4 out of 6 healthy infants (no mention is made of the findings in one of the infants), it seems very doubtful whether her conclusion is justified. Our own findings show that the proportion of lactobacilli in the stools is diminished, and the proportion of coliform bacilli, and to a less extent of streptococci, increased. Most of the coliform bacilli appear to be of the *Bact. coli* I type and most of the streptococci appear to be of the enterococcus type belonging to Lancefield's group D. Neither of these organisms can be regarded as abnormal inhabitants of the bowel, and their pathogenic rôle might therefore be discounted. The fact, however, that these organisms were found in much the same proportions in the fæces of healthy contact infants in the same outbreaks, while they were present in much smaller proportions in the fæces of healthy non-contact infants in normal maternity homes makes one cautious in adopting such a conclusion. Without further evidence it is clearly impossible to decide whether these organisms were the primary cause of the disease or whether their undue proliferation was secondary to a disturbance of the bowel caused by some other agent. *Proteus vulgaris* was rarely met with, and its causative rôle in the two outbreaks that were investigated can be ruled out.

TABLE III—OUTBREAK B: DISTRIBUTION OF BACTERIA IN FÆCES OF NORMAL CONTACT INFANTS

Type	Oxford (14 infants)			Cambridge (10 infants)			Oxford and Cambridge (24 infants)		
	Samples positive	Per cent. of flora		Samples positive	Per cent. of flora		Samples positive	Per cent. of flora	
		Limits when present	A.M.		Limits when present	A.M.		Limits when present	A.M.
Lactobacilli	12	7–95	66	8	25–96	47	20	7–95	58
Coliform	12	1–100	21	8	3–28	9	20	1–100	16
Strepto-cocci	10	<1–93	11	8	9–91	31	18	<1–93	19
Staphylo-cocci	3	<1–15	1	5	1–17	4	8	<1–17	3
Bacteroides	1	6	<1	..	..	..	1	6	1
Clostridia	4	<1	<1	..	..	..	4	<1	<1
Diph-theroids	..	..	..	3	16–42	9	3	16–42	4

TABLE IV—OUTBREAK B: DISTRIBUTION OF BACTERIA IN FÆCES OF SICK INFANTS

Type	Oxford (10 infants)			Cambridge (12 infants)			Oxford and Cambridge (22 infants)		
	Samples positive	Per cent. of flora		Samples positive	Per cent. of flora		Samples positive	Per cent. of flora	
		Limits when present	A.M.		Limits when present	A.M.		Limits when present	A.M.
Lactobacilli	9	9–98	71	11	5–87	50	20	5–98	60
Coliform	9	1–91	22	11	10–100	38	20	1–100	31
Streptococci	4	<1–10	2	5	2–28	5	9	<1–28	4
Staphylococci	5	<1–22	5	2	2–58	6	7	<1–58	5
Clostridia	5	<1	<1	..	..	..	5	<1	<1
Other organisms*	..	..	..	3	4–6	1	3	4–6	1

* Other organisms were proteus and yeasts.

(3) *Infection with a pathogenic organism that does not develop readily in culture.*—Though the media we used are able to grow most organisms that are likely to be met with in the intestine, it is possible that some pathogenic organism may have been present in the fæces of the sick infants which failed to develop under the cultural conditions we were employing. We do not regard this as probable, since if such an organism had been present in anything but small numbers, it would probably have been detected in the direct smear examination. Nevertheless, in any future investigation the greatest variety of culture media and of cultural conditions should be employed in the hope of detecting some organism whose requirements are different from those of the more usual pathogenic intestinal bacteria.

(4) *A toxin formed by an organism in the intestine.*—The occurrence of dysentery in newborn lambs due to the formation in the intestine of a powerful toxin by *Cl. welchii* type B affords a strong analogy for the possibly similar causation of neonatal diarrhœa in human infants. This line of investigation seemed all the more promising since Kimberley (1939) had recently reported the finding of *Cl. welchii* as the predominant organism in the stools of infants suffering from neonatal diarrhœa. Our attempts to confirm this hypothesis, however, met with complete failure. Anaerobic organisms were seldom found, and then only in small numbers. Moreover, the direct examination of the fæces for soluble toxins to mice proved negative. The possibility that a toxin was formed by *Staph. aureus* in the intestine seemed very unlikely, since these organisms were rarely found. The formation in the intestine of toxic split-products from one of the milk proteins by a bacterial species, or combination of species, not generally considered pathogenic must also be envisaged, but so far we have no evidence to support it.

(5) *A bacterial toxin ingested with the food.*—*Staph. aureus* is a not uncommon cause of acute mastitis in cows. The milk may contain an enterotoxin formed as the result of the growth of the staphylococci in the udder, though more usually the toxin is not present in sufficient quantities to be detectable till the milk has been left for a few hours at a suitable temperature after withdrawal (Barber 1914, Crabtree and Litterer 1934, Shaughnessy and Grubb 1936). It seemed not impossible that an enterotoxin-producing strain of *Staph. aureus* might gain access to a maternity ward, infect the breasts of some of the mothers, and lead to the development of toxicity in the milk. This hypothesis received some support from the finding in outbreak C that a number of strains of *Staph. aureus* isolated from the milk of a tuberculin-tested herd supplying the hospital were able to produce an enterotoxin. It received further support when we found that a number of the mothers of sick babies in outbreak B were secreting milk containing pathogenic *Staph. aureus*. When we examined these strains, however, by the kitten test, none of them was found capable of forming an enterotoxin. Moreover, subsequent observations showed that coagulase-positive strains of *Staph. aureus* are frequently present in the milk of healthy mothers with healthy babies. While we would not like to exclude the hypothesis of toxin formation by staphylococci or some other organism in the maternal breast, we must admit that the evidence so far available is far too meagre to justify our regarding it as more than a possible cause in some outbreaks.

(6) *Secondary to a systemic infection with an unknown organism.*—It is possible that the diarrhœa may result from general toxæmia due to infection of some part of the body other than the intestine, such as the middle ear or lung. No opportunity was afforded at Oxford or Cambridge of exploring this suggestion, but the results of examinations made locally as well as the findings of other workers do not seem to lend it much support.

(7) *A virus infection.*—To the best of our knowledge no primary infection of the human intestine with a virus has so far been described, though in certain virus infections of animals, such as rinderpest of cattle and ectromelia of mice, extensive invasion of the intestine may occur. The high degree of infectivity of neonatal diarrhœa is consistent with a virus causation, and this possibility should be kept in mind in any future investigation. In only one outbreak was post-mortem material examined for the presence of viruses—by Dr. van den Ende and Miss Dora Lush—and the results were entirely negative. Prof. James McIntosh has suggested in conversation that the condition may be due to infection of the parasympathetic ganglia with a neurotropic virus leading to increased peristalsis. This suggestion again should be borne in mind in any future investigation, but the very short incubation period of the disease in some cases is slightly against it.

(8) *Infection with a protozoon.*—*Giardia intestinalis* and certain other protozoa are responsible for enteritis in children, and it is conceivable that neonatal diarrhœa may be primarily a protozoal infection. Although this possibility cannot be entirely excluded, it may be noted that examination at Cambridge of unstained films of fæces from outbreaks A and B failed to reveal the presence of any protozoa.

Other hypotheses might be suggested, but to no particular purpose. The comparatively mild disturbance in the normal bacterial flora of the intestine in infants suffering from neonatal diarrhœa—a disturbance that may easily be due to the more rapid passage of food through the intestine with consequently insufficient time for the lactobacilli to proliferate in the lower bowel—suggests that the disease is not due to the prodigious multiplication of an abnormal bacterium gaining access to the intestine. The relatively insignificant post-mortem findings, both macroscopic and microscopic, are suggestive more of a toxæmic condition or a virus infection than of a primary bacterial enteritis.

From a bacteriological point of view it is entirely possible that neonatal diarrhœa is not due to a single pathogenic agent. The diverse findings that have been recorded in this disease (see opening paragraph of this article) are curiously reminiscent of those in summer diarrhœa of children, in which the predominant organism in different countries of the world has been found to be *Bact. shigæ*, *Bact. flexneri*, *Bact. sonnei*, a member of the salmonella group, *P. vulgaris*, *P. morgani*, *Pseudomonas pyocyanea*, or *Cl. welchii* (see Topley and Wilson 1936). The gastro-enteritis of infants that have passed the neonatal period, which has recently been described by Dobbs (1941) as the greatest menace to infants with pyloric stenosis admitted to English hospitals, likewise remains of uncertain ætiology. It may be that all these different diarrhœal complexes are of similar causation, and are due to (*a*) a primary virus infection or (*b*) some systemic bacterial infection or metabolic disturbance, either or both of which paves the way for the proliferation in the intestine of any pathogenic or potentially pathogenic organism that happens to be present. In this connexion it may be that organisms which are non-pathogenic to adults may under favourable conditions assume pathogenicity for infants and young children.

CONCLUSIONS

1. Though it would be unjustifiable to draw any definite conclusions from the limited material we have examined, there seems no evidence to suggest that organisms of the salmonella or dysentery groups are concerned in neonatal diarrhœa.

2. There is no evidence of the formation of soluble toxic substances by anaerobic bacilli in the intestine, analogous to what occurs in lamb dysentery.

3. There is no evidence of the formation of toxic substances under bacterial action in the maternal breast, though this possibility cannot be excluded.

4. The fact that the fæcal flora in diseased infants differs only slightly from that in normal infants under similar environmental conditions suggests that neonatal diarrhœa is not ordinarily caused by an abnormal organism gaining access to the intestine and multiplying prodigiously.

5. It seems more probable that neonatal diarrhœa results from either (*a*) a virus invading the intestine, or possibly the parasympathetic ganglia, and giving rise to increased peristalsis; or (*b*) a systemic infection, intoxication, or general metabolic disturbance leading to the proliferation of any pathogenic or potentially pathogenic organism that happens to be present in the bowel.

SUMMARY

Normal infants.—A quantitative cultural examination was made at Oxford and Cambridge of the fæcal flora of 57 normal non-contact breast-fed infants, 3–23 days of age, in maternity homes free from neonatal diarrhœa. On the average *Lactobacillus bifidus* was found to constitute about 80% of the organisms, coliform bacilli about 10%, and streptococci and staphylococci each about 4%. Members of the clostridium group and of the bacteroides group were found infrequently, and then in only small numbers. The proportions, however, in which the different organisms were present was subject to great variation from infant to infant. Most of the coliform bacilli belonged to the *Bact. coli* I type, and most of the streptococci to the enterococcus type. *Staph. albus* was found in rather more than half the infants, but *Staph. aureus* was isolated only once.

Infants with neonatal diarrhœa.—The fæcal flora was studied in two outbreaks, a total of 34 infants being examined. The proportion of lactobacilli was reduced to 30 and 60%, and the proportion of coliform bacilli increased to 55 and 31% respectively. Very similar changes, however, were found in control healthy contact infants during the same outbreaks. The proportion of streptococci and staphylococci showed but little change. Organisms of the clostridium and bacteroides groups were seldom present. No organisms of the salmonella or dysentery groups were found, and no evidence was obtained of the existence in the stools of soluble toxins for mice. In one outbreak *Staph. aureus* was isolated from the milk of a number of mothers with sick children and was found to be coagulase-positive and hæmolysin-positive. None of the four strains studied, however, was able to form an enterotoxin. On the other hand, four strains isolated in connexion with another outbreak from the milk of a tuberculin-tested herd supplied to the hospital were found to be coagulase-positive, hæmolysin-positive, and enterotoxin-positive.

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NEPHRECTOMY IN UNILATERAL RENAL DISEASE WITH HYPERTENSION

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THE association between renal disease and hypertension is well recognised. In view of this it seems that cases of hypertension without clinically obvious renal deficiency are too often grouped as essential hypertension. Schroeder and Steele [26] investigated 71 cases diagnosed as essential hypertension and found that 50 showed abnormalities of the urinary tract, 38 being unilateral. Of 600 cases of hypertension, Maher and Wosika [17] demonstrated urological disorders in 101.

In cases which have unilateral renal lesions amenable to surgical treatment, it is clearly of value to study the effects of therapy on the hypertension with a view to discovering possible ætiological agents. We have recently had the opportunity of studying 2 such cases.

CASE-HISTORIES

CASE 1.—A man, aged 35, was admitted complaining of frequent attacks of left-sided renal colic. About 4½ years before he had severe headaches and morning epistaxis, and a few months later was admitted to hospital for difficulty in walking and partial aphasia. There he was found to have a right hemiplegia and a blood-pressure of 200/130 mm. Hg; his urine contained albumin but no red cells or casts; his blood-urea was 26 mg. per 100 c.cm. The symptoms disappeared with rest and he was discharged as a case of essential hypertension. Two years later he was again complaining of headaches and epistaxis, but also of pain in the left loin which gradually increased in frequency and severity until he was readmitted to hospital on Aug. 19, 1940. Examination showed slight involuntary movements of the right hand with increased deep reflexes in the arm and leg on that side and absence of the right abdominal reflexes; there was a right extensor plantar response. The pulse was regular; the blood-pressure varied from 235/140 to 245/140. There was slight enlargement of the heart to the left and an accentuated aortic second sound. Urine: albumin present; numerous pus cells, a few red cells and cellular casts. Blood-urea 30 mg. per 100 c.cm. A radiogram showed opacities in the left renal area and intravenous pyelography localised these to the renal pelvis. There was deficient excretion on the left side, but normal excretion on the right side.

Nephrectomy was performed by Mr. N. Hodgson on Sept. 2. At the lower pole the kidney substance was largely replaced by caseous material; in the mid-zone there was a tuberculous focus completely destroying an area about 3 cm. in diameter. The pelvis was not dilated. At the upper pole there was one area suggestive of hypertensive renal atrophy. Histological examination showed active renal phthisis. Outside the tuberculous areas there was an occasional sclerosed glomerulus, otherwise the glomeruli showed dilatation of the capsular spaces. Some of the arterioles and a branch of the renal artery at the hilus showed muscular hypertrophy.

The patient made a rapid recovery from the operation and there was immediate symptomatic improvement. He was discharged from hospital on the 14th postoperative day, and has been seen at intervals in the succeeding 7 months. While in hospital, and at his subsequent visits, the blood-pressure was taken under standard conditions. After a transitory fall to below normal levels, as a result of postoperative shock, the pressure was maintained at a normal level for a time, and then rose slightly to the region of 150/100, where it has remained. When last seen, hypertensive symptoms had completely disappeared, and the patient has joined the N.A.A.F.I. and is prepared for foreign service.

CASE 2.—A man, aged 55, was admitted to hospital complaining of a dull aching pain in the right loin of one week's

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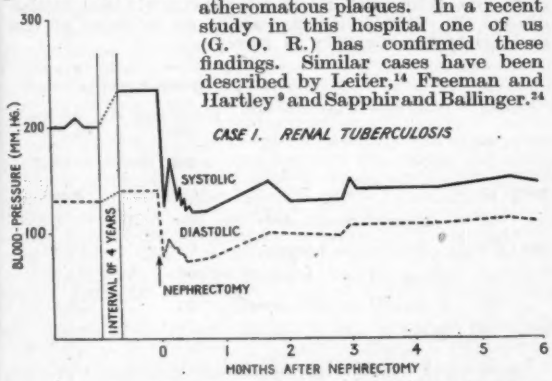
duration. He had also noticed blood in his urine with occasional small clots. A mass was felt in the region of the lower pole of the right kidney. The blood-pressure varied from 195/105 to 185/95. Cystoscopy and retrograde pyelography were performed on March 3, 1941. The right ureteric orifice was inflamed and pouting; the radiogram showed a filling defect of the right renal pelvis and major calyces. Nephrectomy was performed by Mr. W. A. Hewitson on March 10, 1941. More than half the kidney substance was replaced by yellow tumour nodules with numerous areas of hæmorrhage; the main renal vein at the hilus was almost occluded by tumour. The histological appearances were typical of hypernephroma.

The patient made an uninterrupted recovery. The blood-pressure declined to 130/80, and has remained at this level.

DISCUSSION

The relation between hypertension and a coincidental unilateral renal lesion is best demonstrated by the result of removal of the affected kidney. We have been able to find 28 previously reported cases. [1 2 5 6 7 8 13 16 19 20 21 23 25] An analysis of these cases shows that they fall into four groups, each of which has its experimental counterpart.

1. *Renal arterial occlusion.*—Goldblatt and his collaborators [10] have shown that partial occlusion of the main renal artery produced hypertension. Leadbetter and Burkland [13] have recorded a case in a child with hypertension in which nephrectomy was performed for a ptosed kidney, the renal artery of which was found to be partially obstructed by a smooth-muscle tumour. The operation resulted in a cure of the hypertension. In an examination of autopsy material, Blackman [4] has shown that in most cases with essential hypertension there is partial occlusion of one or both main renal arteries by atheromatous plaques. In a recent study in this hospital one of us (G. O. R.) has confirmed these findings. Similar cases have been described by Leiter,[14] Freeman and Hartley [9] and Sapphir and Ballinger.[24]

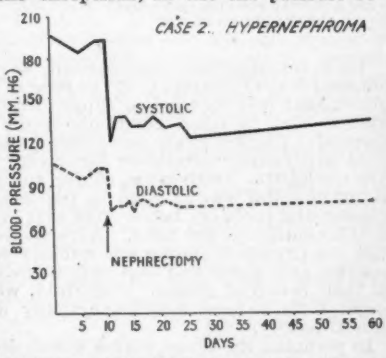


2. *Lesions resulting in partial occlusion of the renal vein.*—Bell and Pederson [3] and Menendez [18] showed that experimental partial occlusion of the renal vein resulted in hypertension. This has been recorded by Perry and Taylor [22] in an autopsy on a child with hypertension apparently due to thrombosis of the renal veins. Our second case is highly suggestive of an ætiological association between partial venous occlusion and hypertension.

3. *Diseases of the kidney substance.*—The association of chronic diffuse nephritis with hypertension is too well known to require further comment. Attention has lately been drawn to the occurrence of hypertension in cases of chronic pyelonephritis, even when the lesion is unilateral.[15] Several cases of this type with successful surgical intervention have been reported, and our first case is another example. Experimentally, chronic interstitial fibrosis of the kidneys produced by X rays has resulted in hypertension.[12]

4. *Lesions causing obstruction to the outflow of urine.*—Harrison and his colleagues [11] produced hypertension by occlusion of one or both ureters. Clinical examples of this type are frequent.

It appears that in most of the cases reported in the literature removal of the diseased kidney has been followed by a substantial and prolonged fall in the blood-pressure. It might be claimed that such a fall would follow any major surgical operation. Volini and Flaxman [27] have investigated the effect of a variety of non-specific operations carried out on hypertensive patients. They have shown that, although in many cases there is definite symptomatic improvement, there is no alteration in the blood-pressure apart from the transitory fall due to postoperative shock. In all except 5 of the recorded cases the blood-pressure fell to 150/100 or lower after unilateral nephrectomy, and remained at this level. Of the exceptions, in one the pressure remained between 140/74 and 160/90 for a considerable time (unstated), but 11 years later it had risen to 190/122[6]; no investigation of the remaining kidney was carried out at that time, so it is possible that it had become diseased. At the time of operation 2 other reported cases [25] showed evidence of diminished renal function in the intact kidney, so it seems probable that they were not cases of unilateral renal disease. In the fourth unsuccessful case, the pathology was not clearly demonstrated.[23] In the case recorded by Mulholland,[19] the lesion (renal calculus) had been present 14 years before, at which time the patient had refused operation. When treatment was undertaken, severe cerebral symptoms were present; these decreased sufficiently after nephrectomy for the patient to do her normal work.



It is premature to speculate about the mechanism whereby hypertension is produced in these cases, but it is clear that a careful investigation of all cases of supposed essential hypertension will reveal many cases with lesions of one kidney amenable to surgical treatment. The recorded cases show that when hypertension is associated with unilateral renal disease relief both of the hypertension and the symptoms will probably follow nephrectomy.

SUMMARY

Two cases of hypertension, one of which had previously been classed as essential hypertension, are reported in which unilateral renal lesions were treated by nephrectomy with significant lowering of the blood-pressure.

Similar cases reported elsewhere fall into four groups showing: renal arterial occlusion; partial occlusion of a renal vein; diseases of the kidney substance; or lesions causing obstruction to the outflow of urine. Each of these has an experimental counterpart.

In view of the therapeutic results and the known association between unilateral renal disease and hypertension, all cases of chronic hypertension should have a complete urological investigation.

We wish to thank Mr. N. Hodgson, Mr. W. A. Hewitson and Dr. J. C. Spence for permission to use the records of the cases which were under their care.

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BLACK-CURRANT PUREE AS A SOURCE OF VITAMIN C

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THIS investigation was started to determine the minimal dose of vitamin C, in the form of a black-currant puree, that was required to supplement adequately the routine diet in some children's wards of an E.M.S. hospital. Black-currant puree was chosen as being the most satisfactory substitute for orange juice available (Olliver 1940). During the winter and spring the diet at the hospital was as good as the local food position allowed and probably better than that of many children in this country at the time. Nevertheless it was found that the vitamin-C intake was unlikely to exceed 5 mg. ascorbic acid a day and that only if the children ate up all their ration of greens. One child, who had been in hospital for several months, actually developed mild clinical scurvy.

In planning the investigation it was decided to adopt the simple technique of Pemberton (1940), owing to the difficulties entailed in collecting accurately over a given period urine from infants and small children in a ward. In the morning the child passes a specimen of urine and is then given a test dose of 50 mg. of ascorbic acid per stone weight. After about 2½–3 hours urine is again passed and the specimen discarded. The urine is passed again about 2 hours later. The ascorbic acid in the first and third specimens is then estimated by the technique of Harris and Ray (1935). An increase of at least 3 mg. per 100 c.cm. is taken to indicate a reasonable degree of saturation.

RESULTS

Fifty-nine children were given a preliminary test and not one gave a positive result. The children were then given a daily supplement either of synthetic ascorbic acid or of black-currant puree. The puree used contained 0·8–0·9 mg. ascorbic acid per g. and was well tolerated even by the youngest children. The usual dose was 50 mg. of ascorbic acid or 1½ oz. of puree (40 mg. of ascorbic acid). Periodic re-tests at about weekly intervals were made to see if any improvement had occurred. In only two out of thirty-five children in the hospital were there any signs of improvement after 9–20 days on the supplement, although healthy children living on a farm selected as a control group on a better diet became saturated in just over a week.

It was then decided to saturate the children with a daily dose of 50 mg. per stone and to re-test at three-day intervals (transport difficulties prevented more frequent testing). Fourteen children became saturated in the first 3-day period, and seven of these had previously been given 40–50 mg. of ascorbic acid daily. Six children took 3–6 days to saturate, and two of these had previously been given ascorbic acid. Six children took over 6 days and one failed to become saturated in 24 days. It is of interest to compare these results with those of Harris (1940). Using a somewhat similar saturation technique he found that subjects having a satisfactory diet gave a positive saturation test on the first or second day of the saturation dose, and that the worse the diet had been the longer was the time taken to obtain a positive result. It will be seen that in many cases the degree of unsaturation was extreme.

Once saturated, the children were given either ¾ or 1½ oz. of black-currant puree daily (20 or 40 mg. ascorbic acid) and were re-tested at intervals of 9–10 days. If saturation was maintained on 1½ oz. then ¾ oz. was tried. Unfortunately many of the children were discharged before the lower dose could be tried, so the attempts to find the minimal maintenance dose of ascorbic acid were only partially successful. The average maintenance dose at different ages was as follows. The results obtained have been expressed as mg. of ascorbic acid per stone recorded at different ages.

Ages	mg. ascorbic acid per stone	Av.
0– 3	11, 13, 17, 8, 16	15
3– 6	10, 4, 14	9
6– 9	6, 4, 7, 6, 7	6
9–12	4, 8, 10	7

It is probable that the actual minimal maintenance dose is less than these figures suggest. It is hoped that further work will produce a more accurate result.

A child of 1½ years with clinical scurvy was investigated in the earlier stage of this work. She was cured by six daily doses of 4 oz. black-currant puree and 1 oz. a day was more than sufficient to maintain saturation.

The diseases for which the children were admitted were various, both surgical and medical, and included such cases as talipes, harelip, mastoid (postoperative), cervical adenitis, asthma, debility, bronchiectasis and subacute nephritis, but by the time the maintenance test periods had been reached all but a few of the children were convalescent, afebrile and free from symptoms. Eight cases either failed to saturate within 9 days or failed to maintain saturation on 40 mg. per day; their diagnoses were: chorea (2), hyperthyroidism (1), ulcerative colitis (2), recurrent pyrexia (1) and cœliac disease (2). The following case is an example of the findings in the majority of cases.

Date	Daily dose of ascorbic acid	Ascorbic acid in urine	
		Before test dose	3–5 hr. after test dose
		mg. per 100 c.cm.	
April 11	None	0·15	None
,, 28	50 mg. (ascorbic acid)	0·8	0·55
May 2–4	200 mg. (in 3 days)	1·1	25·6
,, 13	40 mg. (1½ oz. b.-c. puree)	13	55
,, 23	40 mg. (1½ oz. b.-c. puree)	2·2	29·8
June 2	20 mg. (¾ oz. b.-c. puree)	0·7	24

Age 6½ years; weight 49 lb.; admitted for investigation of state of lungs? bronchiectasis.

The difference in response to the test dose when saturation is attained is striking. The ascorbic-acid content of the first specimen of urine before the test dose has very little value as an index of saturation, for unless an excess is being given, the urine contains little or no ascorbic acid.

DISCUSSION

This experiment is only a preliminary survey and the conclusions reached are only approximately correct. There are three sources of error, the first two of which we believe to cancel out the third. The first is the variable amount of ascorbic acid taken in the diet—this has been assessed at 5 mg. daily and ignored. The second is the effect of the test dose given at irregular intervals, never less than 10 days and often as much as 21 days. This would, of course, increase the minimal maintenance dose, but the amount cannot be calculated, as the excess over the saturation requirements is rapidly excreted; in effect this means that the subject starts every new test period freshly saturated and with an unknown but small amount of ascorbic acid in hand. The third error is due to our inability to complete the full test in every subject by finding the level at which saturation is not maintained. In most cases, however, the response to the test dose was definitely smaller on the lower dose, indicating a decrease of the saturation level, and thus there was reason to consider that the minimal maintenance dose had been reached to within a few milligrammes.

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SUMMARY

Convalescent children in a children's ward were saturated with ascorbic acid. Ascorbic acid in the form of black-currant puree was then given as a dietary supplement and the level at which saturation could be maintained was determined by the urinary response to a test dose of ascorbic acid. The level of the daily dose was found to vary from 15 to 6 mg. per stone according to age, corresponding to average daily doses of 1½–2 oz. puree per child.

Our thanks are due to Dr. Janet Gimson and the ward sisters and staff for help in collecting the specimens; to Messrs. Chivers for supplies of black-currant puree and to Miss Mamie Olliver for some analyses and advice.

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LUPUS ERYTHEMATOSUS AND TUBERCULIN TESTS

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THE ætiology of lupus erythematosus is still in dispute. Some authorities regard it as always a tuberculide, some as always a result of focal sepsis; some think it may be either one or the other, some blame an undiscovered organism, and some suggest that the toxin of either the tubercle bacillus or a streptococcus has sensitised the skin to light. This last explanation should mean that the condition is simply an actinic dermatitis. If so, why should light produce the peculiar lesion of lupus erythematosus? And why should two entirely different organisms produce the same unique bizarre and—in general practice—rare lesion? It is easy to understand that different causative factors might produce dermatitis or erythema, but this lesion is distinctive. Can more than one organism produce a gumma?

In my opinion lupus erythematosus is due to an innate characteristic of the skin, usually congenital but sometimes acquired, which renders it peculiarly susceptible to the action of mild tubercle toxin. The action of the toxin is aggravated by irritation, which may be extrinsic (heat, cold, friction, injury or light), or intrinsic (sepsis or worry). The irritation produces a secondary specific toxin which actually causes the lesion and I believe this toxin to be of the nature of a mild slowly acting caustic.

These opinions are based on the results of tuberculin testing in a series of 148 cases of lupus erythematosus (including 3 of the disseminated variety) and 240 people with healthy skins or other dermatological conditions. All the patients, except one aged 14, were adults. The

TABLE I—RESULTS OF MANTOUX TEST IN 86 CASES OF LUPUS ERYTHEMATOSUS AND 140 CONTROLS

Strength of old tuberculin used	Lupus erythematosus		Controls		
	Cases	Positive	Diagnosis	Cases	Positive
1/100, 1/1000, 1/10,000	24	15 (62·5%)	Miscellaneous dermatoses	20*	8 (40%)
1/500, 1/1000	17	14(82%)	,,	24	4 (16·6%)
1/1000 ..	25	19(76%)	,,	32	5 (16%)
1/600, 1/650; 1/660, 1/700, 1/750	20	15(75%)	,,	34	5 (15%)
			Psoriasis	10	3 (30%)
			Tuberculides	10	6 (60%)
			Healthy skin	10	0
Totals ..	86	63(73%)	—	140	31 (21·5%)

* Including 2 tuberculides.

results are shown in tables I and II. In addition, simultaneous Mantoux and Lederle tests were carried out on 300 cases of miscellaneous dermatoses, including 6 tuberculides. Of the 300, 61 (20%) gave a positive Mantoux test and 56 (19%) a positive Lederle test.

It will be seen that altogether 105 of the 148 cases of lupus erythematosus gave a positive tuberculin reaction (71%), compared with 43 of the 240 controls (18%). Moreover, a tuberculous history—old tuberculous glands, healed phthisis, or tuberculosis in the family—was commoner among the cases of lupus erythematosus than among the controls. In one patient the lesions of lupus erythematosus were seen alongside and merging into the tuberculous lesions of Bazin's disease; other observers have reported them in association with lupus vulgaris.

The incidence of sepsis was no commoner among the cases of lupus erythematosus than among the controls. Moreover, sepsis is too common and lupus erythematosus too rare for sepsis to have any important ætiological significance. On the other hand, where septic foci are found in cases of lupus erythematosus they might easily be primarily tuberculous foci in which secondary infection has obscured the picture. I performed "septic" tests, analogous to the Mantoux test, in a small series of cases, but failed to demonstrate any increased sensitivity to the toxins of septic organisms. Thus I tested 24 cases of lupus erythematosus with the toxins of three organisms, used separately—those of *Streptococcus hæmolyticus*, *Strep. viridans* and a staphylococcus. Only one patient responded, giving positive reactions to *Strep. hæmolyticus* and the staphylococcus. Among 20 controls, too, only one patient responded, giving a positive reaction to the hæmolytic streptococcus but to neither of the other two organisms. I then used a mixture of all three toxins on

TABLE II—RESULTS OF LEDERLE (VOLLMER) TUBERCULIN PATCH TEST IN 62 CASES OF LUPUS ERYTHEMATOSUS AND 100 CONTROLS

Lupus erythematosus		Controls		
Cases	Positive	Diagnosis	Cases	Positive
—	—	Miscellaneous dermatoses	80*	12 (15%)
62	42 (67·7%)	Healthy skin	20	0
		Total ..	100	12 (15%)

* Including 2 tuberculides.

16 other cases of lupus erythematosus, none of which gave a reaction, whereas there were 8 positive responses in a group of 48 controls.

Various causative factors have been suggested by different investigators, but countless people have one or more such factors operating strongly without developing lupus erythematosus. Further, in other dermatoses alleged to be due to toxins—pemphigus, for example—the mucous membranes are affected; in lupus erythematosus the mucous membranes are rarely attacked primarily and I think this also points to an innate susceptibility on the part of the skin.

In my view the ætiology of the condition has the following sequence:—

Congenital predisposition → tuberculous toxin → some form of irritation → secondary toxin → lupus erythematosus.

The endotoxin of the tubercle bacillus is incriminated rather than the bacillus itself because Koch's bacillus is not found in the lesions on microscopic examination, nor are tubercles present. Light has been assigned a share in causation by some because the lesions of lupus erythematosus appear on exposed areas; these areas, however, are exposed to general and constant irritation from various factors including light, so that "exposed parts" can be taken to be synonymous with "irritated parts." Finally, it seems to me that only a substance with a cauterising action could produce the characteristic lesions and this I believe to be produced in the congenitally susceptible skin as a result of irritation.

SUMMARY

A series of 148 cases of lupus erythematosus and 240 people with normal skins or other dermatological conditions were submitted to Mantoux or Lederle tuberculin tests; 71% of the lupus erythematosus cases gave positive reactions, compared with 18% of the controls.

Tests analogous to the Mantoux test were performed with the toxins of three septic organisms—*Strep. hæmolyticus*, *Strep. viridans* and a staphylococcus—on

24 cases of lupus erythematosus and 20 controls. Only one patient in each group gave a positive result. When a mixture of all three toxins was used there were no positive results in 16 cases of lupus erythematosus, but 8 positives in 48 controls.

It is suggested that lupus erythematosus is produced in susceptible people by the action of tuberculous toxin, extrinsic or intrinsic sources of irritation acting as secondary factors.

PREVENTION OF DROPLET-BORNE INFECTIONS BY SPRAY

A FIELD EXPERIMENT

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MAJOR, R.A.M.C.

INCREASING interest has lately been centred on the use of various methods designed to minimise the spread of infections, and the outbreak of war has stimulated research with a view to applying the results of laboratory observations to the treatment of crowded rooms and air-raid shelters. The limitations of the laboratory experiments have been realised by Andrewes,[1] who in the summary of a recent paper says: "We have discovered certain methods for the control of respiratory disease; none of these is of proved efficacy in the field, though all of them have given encouraging results in the laboratory." The necessary field experiments can be carried out most accurately under Service conditions, where large bodies of troops can be surveyed in strictly comparable conditions. With this end in view we carried out such an experiment during the respiratory epidemic period of January–March, 1941.

Two main conditions must be established for the statistical results to be of value. First, the methods used must be so simple that there is a real likelihood of their being effectively carried out by the N.C.O.s charged with the duty, and the materials used must be cheap and readily available; this prevents the use under Service conditions of the more complicated forms of spray and especially of the continuous electrically operated spray. Secondly, a sufficiently large number of men, with an equal number of controls, all equally exposed to the introduction of infection from their contacts with the civil population, and all living under identical conditions of accommodation, clothing, diet and occupation, must be involved in the experiment. The personnel of a searchlight brigade were selected as satisfactory subjects, for, with the exception of a few headquarters personnel occupying buildings, the men were all accommodated in huts under comparable conditions, receiving the same short home leave. The brigade was widely dispersed over a mixed urban, mining and agricultural area of Scotland with fairly equal access to picture houses and other places of entertainment. Thanks to the collaboration of Brigadier A. H. Morton and the regimental commanders the following arrangements were made:

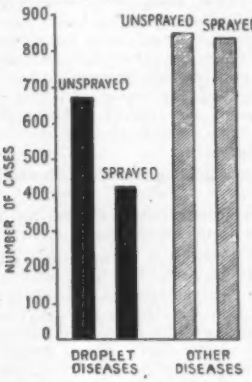

FIG. 1—Total incidence of disease; Jan. 5–April 6, 1941.

Twelve batteries were selected, each battery area adjoining that of its neighbours without any gaps between them. Alternate batteries were sprayed over the whole area, leaving the intervening ones unsprayed. Thus sprayed and unsprayed personnel were fairly evenly distributed over the segment of the British Isles involved. By this means some 3000 men were subjected to spray with about an equal number of controls.

Laboratory investigations have shown that hypochlorite solutions are effective in low concentrations. Hypochlorite was easily accessible to the units in question in the form of the water-sterilising powder actually in use for the treatment of water-supplies. Simple intermittent spraying was therefore carried out in all huts, kitchens, messing-rooms, &c. with an approximately 1% solution of this bleaching powder. The spraying was carried out with the "Flit-gun" variety of sprayer.

Spraying batteries were instructed to spray every hut thrice daily—at reveille, on coming off duty in the late afternoon, and at lights out, these being the periods at which the greatest concentration of salivary droplets may be expected. The Flit-gun container was filled with water and a half scoopful of water-sterilising powder added to it and shaken. The N.C.O. in charge then walked slowly round the hut spraying obliquely upwards towards the ceiling and continued to do so until the whole hut had a quite noticeable but not irritating odour of hypochlorous acid. Complicated methods of control of dosage were clearly out of place and the exact strength of the spray varied because of differences in the construction of different makes of sprayer and deterioration of the solution which is often left in the gun and used again without being freshly made up. The method of spraying to the limit of nasal tolerance for hypochlorous acid is both a simple and practical guide to the unskilled soldier.

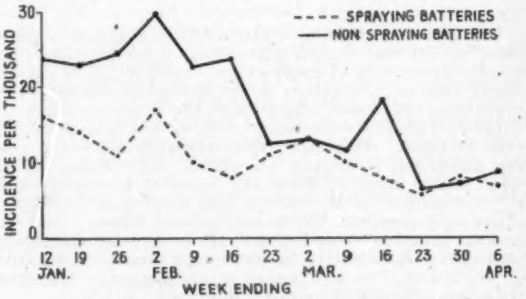

FIG. 2—Incidence of droplet infections per thousand.

The medical officers of both sprayed and unsprayed batteries completed a weekly return to the brigade senior medical officer showing: (*a*) the ration strength of the battery for the week; (*b*) the number of men reporting sick on account of droplet infection; (*c*) the number of cases of sickness from causes other than droplet infections; and (*d*) the diagnoses of all cases of droplet infections. All returns were then correlated by the brigade S.M.O. and shown as incidence per 1000 personnel in sprayed and unsprayed groups. The returns were corrected for variations in strength of batteries.

RESULTS

During the period under review the total number of cases of droplet-borne diseases reporting sick in the sprayed community amounted to 425, compared with 670 in the unsprayed group. The difference of 37% does not merely reflect a difference between the general sick-rate in the two groups, as is demonstrated by the fact that the non-droplet sick-rate in each is almost exactly the same, amounting to 834 in the sprayed and 850 in the non-sprayed (fig. 1). A graph (fig. 2) of cases of droplet infection in each week per 1000 personnel shows that the difference between sprayed and unsprayed groups is greatest during the period of maximum incidence of droplet-borne disease. The curves meet at the end of the experimental period when epidemics of influenzal colds had died down. It is significant that the outlines of the two curves follow each other fairly closely.

There were no complaints of damage to clothing or metal parts of weapons by the bleach spray. Sprayers of various makes but of similar design were used and it was found that some of them became unserviceable by rust on plungers and corrosion of containers. The better, but not necessarily more expensive, type of sprayer has a piston and piston shaft constructed of rustless material. The well-constructed container of galvanised iron which is associated with this will stand up to the corrosive effect of bleach solution for one season in most cases. In the event of spraying being used on a large scale a non-corrodable material should be used.

1. Andrewes, C. H. *Lancet*, 1940, **2**, 770.

MODE OF ACTION

In an attempt to determine how the spray acts, the assistance of Dr. C. P. Stewart was enlisted and an apparatus was constructed to aspirate a measured volume of air (about 20 litres) through a solution of potassium iodide to detect chlorine by the liberation of iodine. The apparatus is capable of detecting 0·01 mg. of chlorine in the volume of air taken. The door and windows of the hut were closed and spraying carried out by the N.C.O. in the normal manner. The air drawn through five minutes later showed no detectable amount of chlorine in spite of the fact that a definite odour of hypochlorous acid persisted. It was observed that the spray droplets appeared to settle rapidly and to dry off on floor walls and window ledges. Dust from these situations was accordingly tested with potassium iodide and starch and in every instance showed the presence of available chlorine. Later experiments under laboratory conditions showed that chlorine could be detected from the dust up to six hours after a single spraying. From these observations several modes of action may combine to produce beneficial results.

A sedimentation effect by spray droplets entangling and carrying down with them the smaller infected salivary droplets.

A direct sterilising effect on the organisms suspended in these droplets.

A further temporary effect in laying and sterilising organisms in dust on the floor.

A slow continuous action by the release of chlorine from the fine deposit of bleaching powder spread over the hut, persisting until renewed by the next routine spraying.

DISCUSSION

At first sight the 37% reduction in the incidence of droplet-borne disease in the sprayed groups looks significant but a detailed study of the figures from individual batteries makes it less convincing (see table).

INCIDENCE OF SICKNESS IN INDIVIDUAL BATTERIES, CORRECTED FOR STRENGTH OF BATTERIES

SPRAYED			UNSPRAYED		
Battery	Non-droplet diseases	Droplet diseases	Battery	Non-droplet diseases	Droplet diseases
A	68	71	G	109	182
B	135	48	H	251	223
C	158	61	I	174	77
D	145	65	J	120	43
E	108	85	K	110	82
F	220	95	L	86	63
Total	834	425		850	670

It is evident that the figures for G and H Batteries in the unsprayed group are largely responsible for the apparent differences between the groups and that if these two batteries were neglected the incidences of droplet disease would be approximately the same in the sprayed and unsprayed group. The figures for G and H Batteries may be explained on one of the following hypotheses: (*a*) A local condition in the batteries concerned, such as a slack or over-conscientious medical officer, a poor level of general health, or low morale among the troops; or (*b*) an epidemic of catarrhal disease involving these two batteries. If any local conditions had been responsible the level of non-droplet sickness in these two batteries should have been correspondingly high. This is not so. H Battery, with a very high non-droplet and droplet rate, may usefully be compared with F Battery in the sprayed group which shows an almost equally high non-droplet rate with a reasonably low droplet rate. G Battery's non-droplet rate is not abnormally high and it is interesting to compare it with the figures of D Battery in the sprayed group. G and D Batteries belong to the same regiment, occupying adjacent areas of a strictly comparable rural type of country, without special exposure to infections. G showed a very high droplet rate while D, with a much higher general-sickness rate, had roughly a third of G's droplet rate. The conclusion is that the high incidence in G and H Batteries is the result of local epidemics of catarrhal disease. It is perhaps significant that two out of six unsprayed batteries suffered in this way while none of the sprayed batteries, even though in areas closely adjacent to the affected batteries, were involved.

SUMMARY

A controlled experiment using the most elementary and simple form of spraying with a hypochlorite solution affords some evidence that this method is capable of diminishing the spread of droplet-borne infections within a unit. The method achieves its best results during epidemic periods.

We are indebted to Major J. L. Cowan, R.A.M.C., for assistance in the earlier stages of the investigation and to the regimental medical officers of the brigade without whose coöperation this experiment could not have been carried out.

BIOPSY OF THE ENDOMETRIUM

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FOR some years American gynæcologists have been obtaining biopsy specimens of the endometrium for histological examination without anæsthesia as an out-patient examination. In this country a small number of gynæcologists have adopted this practice, and it is the purpose of this communication to put on record my experience of 238 biopsies in 84 patients over a period of a year at St. Bartholomew's Hospital in the hope that the safety and efficacy of this simple and convenient method of investigation may recommend it to others. The number of cases is not great, since the war curtailed the work, but the figures are adequate for the conclusions drawn.

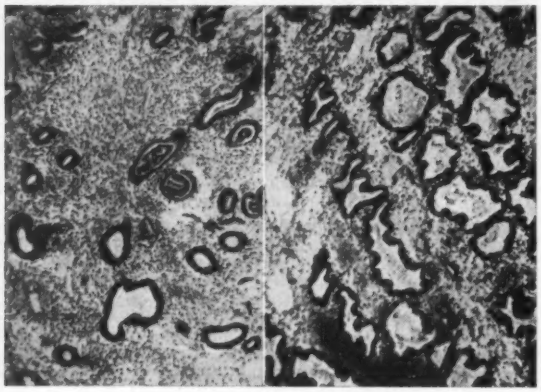
Most curettage operations are undertaken for purposes of diagnosis; but if exact information of the behaviour of the endometrium is to be obtained it is important that the curetting be done at a definite phase of the menstrual cycle. Pressure on hospital beds and the size of the waiting-list seldom allow of this exact timing, and often the bed is wasted and the patient is submitted to an operation the results of which are fruitless. Another small point is that the operation is often performed by a junior colleague or house-surgeon who does not know the exact reason for the curettage and who, from inexperience, may obtain a specimen—possibly from the isthmus or endocervix—which is inadequate for histological study. Endometrium most representative of the whole may best be obtained at the fundus, and after a little practice an operator of average dexterity will almost always procure his specimen from this region; moreover, he will know by inspection whether he has secured a useful piece or must explore a second time. In this way, always seeing the same cases and always operating himself, he is sure of the exact continuity of his specimens which is essential in diagnosis and in the ultimate histological assessment of the results of any given endocrine therapy.

There are at present two methods whereby one may obtain exact information about a woman's menstrual cycle—by serial biopsy of her endometrium, and by biological assay of her hormones, either circulating in the blood-stream or excreted as end-products in her urine. The estimation of urinary pregnandiol is a good example of such biological assay, and its presence at a given time in a given quantity is at least presumptive evidence of ovulation and corpus-luteum formation. This evidence becomes more than presumptive if a biopsy specimen taken in the last week of a 28-day cycle shows an endometrium with well-marked secretory-phase changes in the glands and stroma. As a positive check on the efficacy and the dosage of hormone therapy endometrial biopsy is again extremely valuable, and in many cases in this series it has made it possible to demonstrate œstrogenic and secretory changes in the endometrium where a previous serial biopsy had shown them to be deficient or absent. The method must never be used in an attempt to diagnose malignant disease in the cavity of the uterus. Endometrial biopsy as performed on outpatients has considerable advantages from an economical point of view. An examination that would

entail the use of a hospital bed for a month, and immobilise a woman who may be extremely unwilling to leave her family or her job, can be carried out in this way equally well and perhaps better without admission to hospital; crowded gynæcological waiting-lists are thus kept free for the more urgent hysterectomies and prolapses.

TECHNIQUE AND RESULTS

The present series consists of 84 patients: 44 cases of sterility, 31 cases of irregular uterine bleeding and 9 cases of amenorrhœa. The total number of biopsies performed in these women was 238, the average number being 2 or 3 in each case and the highest individual score 10; several had 5, 6 or 7 biopsies.



(*a*) (*b*)

Biopsy specimens of endometrium. (*a*) Œstrogenic, (*b*) secretory phase.

The technique is simple. At the first examination a careful history is taken and the menstrual cycle should be plotted on a printed menstrual-history case-sheet. A bimanual pelvic examination is made and a vaginal speculum passed, the cervix being inspected to exclude any organic lesion. Any cervical infection is best treated and eliminated before the performance of endometrial biopsy. If the case is suitable for biopsy the patient is asked to attend on the day chosen with reference to her menstrual chart, and it has always been my practice to explain what the examination entails and the reasons for it, thereby ensuring the patient's coöperation and confidence. No shaving of the vulva and perinæum is necessary, but the patient is instructed to have a bath on the morning of operation after cutting the pubic hairs reasonably short. When the biopsy is to be taken she is placed in the lithotomy position; the vagina and cervix are well cleaned and the vagina swabbed out with Dettol. The operator should wear a mask, gown and rubber gloves, which are kept in a special drum in the outpatient clinic. A small Auvard's speculum is introduced and the sister retracts the anterior vaginal wall if necessary. The cervix is grasped with light fine volsella and gently steadied, and a small malleable sound is passed to ascertain the direction and size of the cervical canal; occasionally this is narrow and one or two small dilators may then be passed. A fine sharp curette is introduced and a specimen of endometrium obtained from the fundus.

With practice, the whole proceeding takes only a few minutes and the quicker it is done the less likely is the patient to be worried by it. No special instruments are required and in all these cases a small fine ethmoid curette was used and proved itself a trusty and efficient instrument. No special suction curette was ever used. All the instruments are sterilised by boiling for each case, and if the pressure of work is severe they can be duplicated to save time. After the examination the woman is sent to dress and always interviewed before she leaves hospital to make sure that she is feeling no ill effects. She is also warned to expect a faint show for 24 hours or so and assured that this is normal.

The pain experienced varies in different women. The cervix, like most hollow viscera, can be cut and burned by the cautery with relatively little discomfort in the conscious patient, but she rather resents it being stretched. The passage of a dilator is usually commented on and in some cases complained of as painful, though seldom as severely so; hence it is important to use a small instrument. In two of my cases, both nulliparæ, it was impossible to pass an instrument into the cervical canal and these cases had perforce to be put on the inpatient waiting-list. Needless to say, unmarried or virgin patients are as a general rule unsuitable for biopsy without hospital admission. Considering the series as a whole, pain and discomfort during the operation provided a contra-indication in very few patients. Of other minor ill effects, one patient had a mild syncopal attack and nearly fainted and one was sick. These symptoms occurred in the earlier cases; with increasing experience and dexterity untoward effects were rare.

In assessing the value of this method of investigation the main criterion is the histological information obtained. A biopsy specimen may be said to be satisfactory if it contains a fair-sized piece of endometrium showing the stromal and glandular pattern clearly, so that study of it will definitely place the endometrium in a given category—typically œstrogenic (fig. *a*) or typically secretory (fig. *b*). With a good section there will be no doubt or hesitation in so placing it. In this series 210 of the 238 specimens were classed as good, 18 as adequate, and 10 as useless. In this last class are included those sections which contained no endometrium, or only cervical mucosa. There is a notable improvement in the proportion of good specimens among the later cases of the series and this is of course the result of practice.

SUMMARY

Biopsy of the endometrium has been performed 238 times in 84 outpatients.

It is a simple and safe procedure that can be conducted without anæsthesia or premedication and without remarkable discomfort to the patient.

The technique used is described; it requires no special instruments and only average skill on the part of the operator.

Judged from a histological standpoint, the specimens obtained provided the information required in all but 10 out of a total of 238.

Biopsy of the endometrium provides exact knowledge of the functional state during any given menstrual cycle, and is particularly useful in cases of sterility and irregular uterine bleeding. It also enables a check to be made on the results and dosage of hormone therapy.

It allows of a great saving of time and money to patient and institution.

I wish to thank my seniors at St. Bartholomew's Hospital, Dr. Malcolm Donaldson, Dr. Wilfred Shaw and Dr. John Beattie for their help; and Mr. B. Cambridge, for cutting and staining all the sections.

TOXICITY OF PHENOTHIAZINE

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THE use of phenothiazine (thiodiphenyl-amine) in the treatment of threadworms was first suggested by Manson-Bahr (1940). He recorded successful results in 6 children and 3 adults, and advised that children under four years should be given 1 g. daily for seven days, children between four and eight 2 g. daily for seven days, and adults 8 g. daily for at least five days. de Eds, Stockton and Thomas (1939), who have investigated the pharmacology of phenothiazine, reported that out of 19 patients in whom blood-counts were made before and after medication with phenothiazine, 3 developed an anæmia. These 3 patients had taken a total dosage of 22·4, 28·1 and 19·9 g. respectively; in the third patient the red-cell count dropped from 4,410,000 to 1,570,000, with reticulocytes increased to 35%. No toxic effect on the leucocytes was observed. They discovered no undesirable effects from the drug in the gastro-intestinal tract, kidneys or liver. The 11 patients on whose serum the van den Bergh test was done all showed a positive indirect reaction; this reaction was attributed to the colour of the dye in the blood-serum. They recommend that, in view of its effect on the red cells, the maximum total dose of phenothiazine should not exceed 15 g.

without a rest period. If this dose is adjusted for body-weight it represents less than half the doses suggested by Manson-Bahr for adults and children.

Phenothiazine was sent to me by Dr. C. M. Scott for clinical trial and I have used it, in a preliminary investigation, in 8 children. In one of these (case 1) poisoning occurred.

CASE 1.—Girl, aged 12 years. Weight 78 lb. Referred from the school clinic for treatment of threadworms on July 3, 1941. Phenothiazine 4 g. for seven days prescribed. On July 10 the child was jaundiced with a furred tongue. Her mother stated that for three days she had been ill; her chief symptoms were nausea, anorexia, insomnia and depression. On July 17 jaundice had faded, but she was obviously anæmic and a blood-count showed red cells 2,900,000; Hb. 60%; white cells 8900 per c.mm.; neutrophils 44% (3916), lymphocytes 53% (4717) and monocytes 3% (267). On the 24th, after a week's treatment with iron, a blood examination showed red cells 3,330,000; Hb. 68%; C.I. 1·02; average diameter of red cells 7·6 μ; white cells 4300; platelets 300,000; volume of packed red cells 36·9% of blood-volume; mean corpuscular volume 110·8 c.mm. (normal 78–94 c.mm.; average 86 c.mm.); eosinophil polymorphs, 2% (86); monocytes 2·5% (108); lymphocytes 50% (2150); neutrophil polymorphs 45·5% (1956); neutrophil nuclear index:

Patient	i, 46;	ii, 46;	iii, 8;	iv, 0;	v, 0
Normal	12	25	25	15	4

Red cells show little variation in size and shape; no stippled or nucleated reds seen; reticulocytes number about 10% of the red cells.

Urine.—Acid, no albumin, no sugar, microscopically clear; no blood pigments, &c., present. Van den Bergh negative.

Complete recovery occurred in one month from the onset of symptoms.

The effects of phenothiazine poisoning in this child were shown by the anæmia and jaundice. It is improbable that the jaundice was hæmolytic in origin, since the anæmia was not sufficiently profound for this; moreover, the clinical condition of the child was strongly suggestive of a hepatitis. This toxic effect on the liver has not been previously reported, but it might have been forecasted in view of the chemical structure of phenothiazine. It is well known that substances containing benzene, such as trinitrotoluene, dinitrobenzene, dinitrophenol and arsenobenzene derivatives, are poisonous both to the liver and the blood elements. As has been suggested above, no help in the differential diagnosis of the jaundice can be expected from the van den Bergh test, which gives an invariable positive indirect reaction when phenothiazine is being taken. The blood-picture in this child showed a severe degree of anæmia and a leucopenia, with evidence of active hæmopoiesis in red cells and neutrophils.

Of the other patients treated with phenothiazine, blood examinations were made before and after treatment in 2 and in one there was evidence of a moderate anæmia.

CASE 2.—Boy, aged 5 years. Weight 38 lb. Referred from the school clinic for treatment of nocturnal enuresis on July 24, 1941. He was found to be suffering from threadworms also. His blood examination made before treatment with phenothiazine showed: red cells, 4,600,000 per c.mm.; Hb. 83%; reticulocytes less than 1%; eosinophils 2000 per c.mm. He was given 0·5 g. phenothiazine three times a day for a week. Blood examination then showed: red cells 4,000,000; Hb. 72%; C.I. 0·9; average diameter of red cells 7·6 μ; white cells 7000; platelets 200,000; cell volume 37·5% of blood-volume; mean corpuscular volume 93·75 c.μ. Red cells show relatively little variation; about 3% are reticulocytes. Eosinophil polymorphs 13% (900), neutrophil polymorphs 33% (2320), lymphocytes 51% (3570), monocytes 3% (210).

Urine.—Some epithelial cells. Very few leucocytes present.

No threadworms were seen after four days' treatment, but eosinophils were still high at 900 per c.mm.

Judging by the American series quoted above, poisoning may be expected in a fair proportion of cases if a total dosage of more than 15 g. is administered to adults. This does not include instances of idiosyncrasy which have not yet been reported but which may be expected to occur rarely. Since evidence of poisoning was discovered in 2 of these 8 children, I decided to assess total dosage in future by body-weight. Accepting the American standard of 15 g. for an approximate weight of 150 lb., 1 g. for every 10 lb. of body-weight was used as the total dose. This amount was spread over 3–5 days and if the threadworms had not entirely disappeared a second course was given a week later. More than 20 children were thus treated, several of them required the second course but all of them were declared by their mothers to be free of threadworms. One child was stated to be depressed and another off her food while under treatment. No further evidence of toxicity was discovered until the last case of the series.

CASE 3.—Girl, aged 2½ years. Referred from the school clinic for treatment of threadworms. Weight 29 lb. Phenothiazine 1 g. for three days prescribed. On the second day of treatment the child was sick and lacked appetite; on the third day the mother noticed that the child was yellow. The next day, on examination, jaundice was confirmed; the liver was enlarged to just above the umbilicus and appeared tender; the urine was red with the excreted dye. Blood examination on the fifth day showed: red cells 41,200,000; Hb. 75%; C.I. 0·89: average diameter of red cells 7·55 μ; white cells 9300; platelets 400,000; eosinophil polymorphs 7%; basophil polymorphs 0·3%; neutrophil polymorphs 24·3%; lymphocytes 63% (5859); monocytes 5·3% (493); neutrophil nuclear index: Patient: *1*, 62; *2*, 30; *3*, 8; *4*, 0; *5*, 0! Normal: *1*, 12; *2*, 25; *3*, 44; *4*, 15; *5*, 4.

A week later the child's general health had improved; her appetite was normal and the liver was smaller but the conjunctivæ were still bile-stained. This child's blood showed a mild anæmia with moderate stimulation of hæmopoiesis. She was undoubtedly suffering from a toxic hepatitis.

EFFICACY OF PHENOTHIAZINE

The employment of a potentially toxic drug in the treatment of a comparatively trivial infestation requires justification. Although trivial, infestation by oxyuris vermicularis is very common; large-scale investigations in lower and middle class white children in Washington D.C. gave a 50% incidence in children from six to eighteen years of age. No comparable investigation has been made in this country; it is a formidable research, because routine examinations of fæces are without value and the eggs have to be sought in peri-anal smears. The ordinary clinical standard of cure is a statement by the mother that she can no longer see threadworms in the child's fæces. This standard is frequently shown to be faulty by the re-emergence of threadworms, sometimes years later. Assessed even by these standards, the uniformly effective drug has not yet been discovered. Hexylresorcinol, as employed in an elaborate technique by Brown (1932), gave complete success judged by the highest standards. Wright and Brady (1940) obtained 60–90% cures in adults and children with gentian violet by mouth. It is probable that Butolan and its more recent equivalents which have been widely used in this country have a comparable efficiency with gentian violet.

It is unfortunate therefore that phenothiazine which appears to be completely successful in the treatment of threadworms should sometimes be toxic to the host even in small doses. Consideration of case 3 suggests that it will be wise in future to restrict its use to cases where less dangerous therapies have repeatedly failed. Its administration should then be strictly supervised.

SUMMARY

Phenothiazine has been shown to be an effective remedy against threadworms in more than 30 cases.

Phenothiazine is poisonous to the blood and the liver in much smaller doses than have been suggested for the treatment of threadworms. Three cases of anæmia following its use have already been recorded in the literature and 3 further instances are given here. In 2 children it also produced a toxic hepatitis.

Phenothiazine is probably too dangerous a remedy to be used in the routine treatment of threadworms.

I am grateful to Dr. G. R. Osborn, pathologist to the hospital, for the pathological investigations recorded and to Dr. C. M. Scott, of Imperial Chemical Industries Ltd., who supplied me with phenothiazine.

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INSULIN HYPOGLYCÆMIA

CHANGES IN NERVOUS MANIFESTATIONS

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CHANGES in the symptomatology of insulin hypoglycæmia in diabetics commonly occur as years of treatment go on and insulin reactions may differ so much from the original ones that patients are dangerously unaware of their onset. At first it is almost the rule that patients feel and easily recognise minor premonitory symptoms. These can be ascribed mainly to reactions of the *autonomic nervous system* and are akin to the effect of a dose of adrenaline; indeed they are probably due to an extra secretion of adrenaline produced in an attempt to mobilise stored glycogen into blood-sugar. Such symptoms are general weakness and faintness, tremors, sweating, hot or cold feelings and palpitation. Other early symptoms, less easily explained by hyperadrenalinæmia, are hunger pains, visual disturbances including diplopia, and tinglings, especially of the lips and tongue. Such symptoms occur, if at all, at definite times of the day or night, at the period of maximal insulin action, and are easily recognised and removed by eating 1–3 lumps of sugar. Many conscientious patients even welcome such mild attacks occasionally, regarding them as a sign that their diabetes is well controlled. Such symptoms indicate as clearly as an exact estimation that the blood-sugar is between 50–70 per mg. 100 c.cm. Should such symptoms be unrecognised or neglected, so that glycopenia persists for a long time, symptoms develop which may be classified, roughly at least, as being due to disturbed function of brain and *central nervous system*; these are mental confusion, symptoms exactly simulating alcoholic intoxication, muscular twitchings, convulsions, epileptiform seizures, transient hemiplegias and complete coma. All these effects disappear rapidly, and usually completely, on restoration of the blood-sugar; but they occasionally persist longer, especially if hypoglycæmia has lasted for one or more hours, and, very occasionally, there is permanent hemiparesis or mental impairment with definite histological changes in the nerve-cells. A few patients never feel early premonitory symptoms but experience the more serious group of symptoms from the start; yet considering the large number of stupid or careless patients on insulin treatment, serious attacks and sequelæ are exceedingly rare.

As years of insulin life go on, sometimes only after 5–10 years, I find it almost the rule that the type of insulin reaction changes, the premonitory autonomic symptoms are missed out and the patient proceeds directly to the more serious manifestations affecting the central nervous system. This applies to diabetics who have been continuously on unmodified soluble insulin as well as those who have been changed to protamine insulin, whose different, slower and more prolonged action often modifies the type of reaction. The following are typical of the changes I refer to. A patient, instead of becoming shaky, sweating, or hungry if his meal is unduly late, becomes suddenly confused and obstreperous, creates a scene and refuses sugar. Another, accustomed to drive a car and usually warned of hypoglycæmia by slight diplopia, becomes suddenly wild and unbalanced in his driving. Yet another, instead of being wakened at night by violent palpitations—his warning to take sugar—goes straight into convulsions and awakens so paralysed that he cannot reach his sugar. The same patient may at one time experience early premonitory symptoms and at another be quite unaware of an inpending attack. It is obvious that these are serious dangers.

I can offer no satisfactory explanation of this change of symptomatology and the common failure of autonomic warning symptoms as time goes on. I have noticed how, at the beginning of insulin treatment, patients feel hypoglycæmia symptoms at a higher blood-sugar level—90 to 120 mg. per 100 c.cm.—than later on, when they may not experience the same feelings until the blood-sugar is 40–60 mg. per 100 c.cm. Here we may say that the tissues become attuned to a lower level of sugar concentration. But the condition I refer to occurs in patients who are often hyperglycæmic and only rarely hypoglycæmic. It is no mystery that if the blood-sugar is low for long enough the central nervous system should react in some untoward way, because if sugar is, as we believe, the only fuel it can use the absence of this fuel must interfere with its vital function. It is also known that the higher cortical functions and centres suffer first and most severely, and that the function and anatomy of the basal ganglia and vital centres are rarely affected. But none of these facts explains why symptoms of upset of autonomic type fail to give warning of trouble as years go on.

I know of no way by which the original sensitivity of the autonomic nervous system can be re-established and the danger of serious hypoglycæmia entirely prevented, but certainly the urine in such diabetics should never be made continuously sugar-free throughout the 24 hours. If they are sugar-free at the time of minimal insulin activity—say after breakfast—they run an almost certain risk of hypoglycæmia at the period of maximal insulin action a few hours later. The most certain way of avoiding trouble in such cases is to give regularly a large carbohydrate buffer (20–30 g. of carbohydrate) before these times of intense insulin action, to anticipate and prevent hypoglycæmic attacks. With soluble insulin this carbohydrate should be given 3 hours after each injection; with protamine insulin it should be given at tea-time if the interval between lunch and supper is a long one, and in all cases at bed-time.

Medical Societies

ROYAL SOCIETY OF MEDICINE

AT a meeting of the Section of Surgery on Nov. 5, with Mr. E. ROCK CARLING, the president, in the chair, a discussion on

Streptococcal Cross-infection in Wards

was opened by Prof. A. A. MILES. Such infection, he said, was an established phenomenon, but seldom gave rise to severe and fatal infections. The common results were cellulitis, erysipelas, extension of wound infection, delayed healing or failure of skin grafts. Of the bacteria commonly taking part *Streptococcus pyogenes* was most easily traced; and though not the commonest cross-infecting organism it was the most important because of its pathogenicity. The incidence of streptococcal cross-infection depended on sources of infection in wounds and upper respiratory passages, on the possible channels of infection, and on the state of the exposed tissues. In the surgical ward of peace-time, the streptococcal reservoir was mainly in the upper respiratory passages, and striking cases of infection were rare. In war-time, wounds infected before admission provided additional reservoirs, and hospital infection was commoner because of this and because of the greater susceptibility of the war wound compared with the operation wound. Poor accommodation and hastily trained staff also played their part. Peace-time technique might prove inadequate to meet the added risks of war. Infection could reach the wound by three main channels—dust, droplets, and transference of organisms on hands and utensils. These possible channels of infection demand separate precautions, which Professor Miles divided into those associated with the actual dressing technique, and others. Among the latter were the use of impermeable masks to prevent droplet-infection, and the exclusion from the ward of anyone with an infected hand or finger. Common utensils should be disinfected every time they were used by an infected patient, and all his things should be kept separate, as far as possible, from those used by other patients. His wound should always be kept covered between dressings. There should be a quiet period in the ward before dressings were begun; bedmaking should cease so that dust could have time to settle. The dressings themselves should be carried out by a team consisting of a trolley attendant who had nothing to do with the patient but simply handed out sterile materials with forceps; a dresser, who used a "no-touch" technique; and an assistant. The dresser and assistant treated each case as a separate unit, washing their hands and having the instruments freshly sterilised between each dressing. They should, if possible, wear fresh dry gloves for each case; the wet scrubbed hand, with infection trickling down from the forearm, should not be

used. Bacteriological surveys often revealed defects in dressing technique. Professor Miles said he had made an investigation, with Dr. Joyce Wright, of the incidence of cross-infection in a ward containing both air-raid casualties and operation cases; during the first period an ordinary dressing technique was used, and during the second the team-technique was used, masking was compulsory, and there was a quiet period in the ward before dressings were begun. Results were as follows:

	Air-raid casualties	Cross-infection	Operations	Cross-infection
1st period	32 ..	10	46 ..	2
2nd „	46 ..	1	49 ..	0

In both periods 10 heavily infected cases were admitted, so that the menace was about the same; but the revision of technique reduced cross-infection from about 15% to 1%. Improved aseptic precautions did not entail an increase of medical or nursing staff, and the speed of teamwork made up for the time lost by employing several people on one dressing. More bacteriologically controlled surveys were needed to test the effect of prophylactic methods, and to establish that cross-infection was important even in wards where its effects were not obvious.

Prof. J. PATERSON ROSS remarked that this "fiddle-faddle" of aseptic technique—as Clifford Allbutt had called it—must be attended to. Simple precautions could be taken against dust and droplet-infection by shutting windows and stopping bedmaking an hour before dressings were due to begin. Receptacles containing dressings should have lids to them, and the wound must be left uncovered for the minimum time. Masks must be not only impervious but large enough to cover the nose and chin and stretch a good way to the sides; they should measure 6 × 8 in. at least. In order to prevent contact infection forceps should be used or gloves worn; hands and instruments should be dry, and the fingers of the dresser should never touch the wound, the skin round it, or the dressings next the skin. Palpation round the wound could be done, if necessary, with a piece of wool held in the forceps; and where it was impossible to dress a wound entirely with forceps—as might happen with an empyema wound—the patient should be taken to the theatre and dressed with full theatre technique. In the wards separate packets of dressings might be used for each patient and opened with forceps on a sterile towel spread on the top of the trolley; the dresser could then take what he needed instead of having it handed to him, and the clean trolley attendant need only hand him the sterilised instruments. All instruments should be boiled; the edge of a cutting instrument was not spoiled if it was properly wrapped while boiling. Two minutes in boiling water sufficed if instruments had been properly washed. Bowls and irrigating cans should be immersed during boiling. Antiseptic solutions should be checked to see whether they were used strong enough and long enough; spirit could not be trusted. These methods were neither new nor elaborate: they were merely a revival of aseptic technique. It was well to try to oil floors and treat blankets to prevent the spread of dust, but if these measures were not practicable surgeons must make sure that dressing drill was properly learned. The wound which failed to heal by first intention was more liable to cross-infection. It was unreasonable, he said, to use a good technique in the theatre, and a bad one in the ward. In outpatient departments, too, all the rules were broken. Surgeons must teach their students that the quick glance at a wound was dangerous, inviting droplet infection. Indeed, any removal of the dressing was dangerous. He thought that in future we must look forward to a special dressing-room opening off the ward. The tendency was to dress wounds too often, as closed-plaster technique had shown. But it must not be forgotten that organisms could get in and out of plaster, and could be disseminated when a plaster was changed. The Medical Research Council memorandum No. 6 suggested that an asepsis officer should be appointed in large hospitals; but Professor Paterson Ross felt that the surgeon in charge of a unit must be responsible for the technique in that unit; he could always count on help from the bacteriologist. To achieve an aseptic conscience was better than being shadowed by an aseptic policeman.

Dr. M. VAN DEN ENDE held that in general surgical wards cross-infection of wounds occurred mainly through contact, and a careful dressing technique would reduce the incidence. In ear, nose and throat wards, or scarlet-fever wards, the upper respiratory tract was of course more liable to be the source of infection. This region, which trapped bacteria from more than 10 cu. ft. of air per hour, was specially likely to harbour organisms if it had recently been the site of an operation. We were not yet clear, he said, about what constituted a danger. If one streptococcus was enough to produce a cross-infection then dust was dangerous; if 1000 streptococci were needed that danger was slight. But there was danger of dissemination by droplets even in a general surgical ward. The nurse with an upper respiratory infection should be sent on leave. Patients with such infections had been shown to deposit large numbers of organisms on the bedclothes near the head, and these were disseminated during bedmaking. Photographs of sneezers showed the distant projection of droplets, and gauze masks might not intercept these. Cellulose-acetate masks should therefore be used. Large droplets carrying infective doses had a relatively short range and fell to the ground rapidly; adequate bed spacing and masking dealt with them effectively. During dusting and bedmaking the number of organisms in the air of a ward were at their peak, and they could remain suspended for long periods. Treatment of the floors and bedclothes with dust-laying oils reduced the numbers successfully. For 1000 sq. ft. of floor 1 gallon of spindle oil was needed. It looked dull, but the nurses got used to it, and if the excess was removed it was not slippery. It was not bactericidal, and no suitable antiseptic had yet been found to mix with it, but efforts were being made to find one. Technical white oil could be used for bedclothes, and could be applied in the hospital laundry. He thought that tests were urgently needed of the value of dust-laying methods in reducing cross-infection, especially in scarlet fever, diphtheria and ear, nose and throat wards.

Colonel LEONARD COLEBROOK described two cases in which a general infection had been acquired from dust. He then traced the events following admission to hospital, in January, 1941, of a patient with severe burns infected with a type 12 streptococcus which was resistant to sulphanilamide. He was nursed in a bathroom 18–19 yards away from the ward first affected, and he ultimately died. Subsequently 14 cross-infections from his organism were identified, in 6 of which skin grafts were lost or went wrong as a result, while in the remainder there was infection of healing wounds, delayed healing or cellulitis. Every effort had been made to check spread—floors had been oiled and gloves and masks worn. The fact that the organism was sulphonamide resistant might have been partly responsible, and it might have other properties which made it particularly invasive. There had been hardly any acute throats in the affected wards. He believed that cross-infection was a bacteriological problem and should be dealt with by bacteriologists, and he favoured the idea of an asepsis officer, believing he could succeed in getting the facts over to students and nurses. If it was left to the surgeons there would be spurts of enthusiasm followed by lapses. It would be better to begin by having imperfectly trained asepsis officers than none at all. They should take the nurses into the laboratory and let them make cultures and learn a little first-hand bacteriology: their interest was a revelation.

Sir JAMES WALTON reminded the meeting that in this war we had had practically no experience of gross infections. Patients with bomb lacerations were operated on as soon as they got over the shock; their wounds were treated with sulphonamide and left for ten days, when they were found to be healing with clean granulation tissue. But if war came into this country we should see gross infections. Every medical officer must learn to adapt himself to what he could get. It was possible to dress wounds entirely without touching them, and thus without washing between cases. A man could not dress 40 cases, washing between each; but he could go round with forceps, using a separate packet of dressings and freshly sterilised instruments for each patient and never touch a wound. He had been inspecting many hospitals and had found none where dressing with forceps was compulsory. Ear, nose and throat cases should not be nursed in general surgical wards.

Dr. W. A. BRADLEY had followed the spread of *Strep. pyogenes* infections in Addenbrooke's Hospital and had found different types prevalent at different times. Thus types 8 and 3 were prevalent in some wards at the beginning of the investigation, but they had then disappeared for some years. At other periods he found types 6 and 22. Outbreaks of a single type would last about three months and spread slowly; often just when a general spread seemed imminent that type disappeared spontaneously. After a time it became possible to tell how a strain came in: type 6, for example, was introduced by a case of cellulitis. He found it hard to suppose that dust or bedclothes infections played more than a minor part in spread. In a public school which he had investigated spread of infection seemed to be related to the placing of beds in the dormitories, not to exposure to dust in playrooms and corridors.

Lieutenant-Commander JOHN BUNYAN said that organisms grown from a wound had no significance unless they were causing symptoms. If the wound was encouraged to heal from the start contamination by bacteria became less important. The use of the Stannard oiled silk envelope made it very difficult for secondary infection to occur. The envelope could be applied immediately by anyone and left in position for three weeks. The wound could be treated by irrigation with electrolytic hypochlorite solution. If the wound was healing well inside the envelope the type of organisms to be found outside became merely academic.

Dr. E. T. C. SPOONER described a study carried out at Hill End Hospital from November, 1940, to April, 1941, inclusive, in a plastic surgery ward. Swabs were taken from wounds and throats, and it was found that 65% of wounds were infected with hæmolytic streptococci, and that a quarter of these infections began while the patients were under observation. In one epidemic due to a type 13 organism, 3 throats and 15 wounds were infected (one wounded man was seriously ill and 4 Thiersch grafts failed). A type 4 epidemic, starting from 5 burns infected with the same organism admitted together from the same hospital, spread to 18 throats and 4 wounds. The type 13 organism had been found by Colonel Colebrook to be resistant to sulphanilamide, whereas the type organism was susceptible to the drug. All wounds were being treated with sulphanilamide powder. This experience illustrated the need for continual investigation which alone could give that fresh insight likely to extend what was known about the control of infection.

Mr. H. W. RODGERS said that he had been attempting to reduce the smell of the closed plaster method of treatment by enclosing a sheet of gauze soaked in strong antiseptic between the layers of the plaster. This, besides preventing the smell from becoming serious for three weeks, retained much of the pus seeping from the wound. He asked whether it would also have an effect in preventing cross-infection. Professor MILES replied that on general principles a layer of strong antiseptic might be expected to reduce the number of bacteria coming through the plaster.

Reviews of Books

Warwick and Tunstall's First-aid to the Injured and Sick

(18th ed.) Editor: NORMAN HAMMER, M.R.C.S., late R.A.M.C., county surgeon, St. John Ambulance Brigade. Bristol: John Wright and Sons. Pp. 336. 3*s.* 6*d.*

THIS is an advanced ambulance handbook. Part 1, on anatomy and physiology, is well written, and gives much more information than that usually found in first-aid textbooks. Part 2 has been largely rewritten, and includes notes on air-raid casualties, war gases, transport and methods of blanketing a stretcher. Busy doctors faced with fallow and inquisitive first-aid classes will welcome it as a reference book. Others may argue that first-aid should never be an advanced subject: that its greatest value lies in its limitations. The great surgeon and the St. John Ambulance man are brothers by the roadside, and perhaps there is a growing tendency today to teach too much in the name of first-aid; reports by competent authorities tell of dangers too. Should we not be wiser in these days of war to teach the greatest number of people the simplest facts of common sense that save life?

The book is full of excellent suggestions and explanations; but ancient illustrations, depicting self-conscious gentlemen of bygone days, have become the depressing but inevitable trade mark of first-aid textbooks. Clear illustrations are an immense help to the student. May we hope in the future for clear line drawings of artistic merit, and more of the type of illustration shown on page 199?

Biologic Fundamentals of Radiation Therapy

FRIEDRICH ELLINGER, M.D., research fellow, radiotherapy department, Montefiore Hospital, New York City; formerly privatdozent in radiology, University of Berlin. London: H. K. Lewis and Co. Pp. 360. 30*s.*

THIS is a comprehensive survey of the literature of all types of radiation used in medicine—ultraviolet light, X rays and gamma rays. The action of radiation on the cell is considered first, followed by an important section in which the action of X rays and gamma rays on the tissues of the human body are described in detail. The effect on the skin is regarded as being of special importance because it was the biological indication used in all the earlier methods of estimating dosage, and because the production of irreversible reactions in the skin limits the dose which can be given through any external portal. Different organs and tissues are considered and much experimental work is quoted. The chapters on the therapeutic uses of radiation are less satisfactory because the task is more difficult. In the last twenty years the science and practice of radiology have been changing so quickly that opinions firmly held a few years before may be regarded as out of date even by the author who originally published the conclusions; and the selection for quotation of work based only on reliable experimental evidence is impossible at the present stage. It is not in line with modern thought, however, to include Hodgkin's disease as an infectious new growth, while the closely related and sometimes indistinguishable lymphosarcoma is mentioned in a short section on sarcoma in general as if it were a neoplasm of the skin only. Dr. Ellinger points out that the doses mentioned are merely given for orientation purposes; but they reflect the confusion in practice, including as they do doses in S.E.D., r in air, r on skin with backscatter, skin doses per field and summated dose, and for radium milligramme hours.

Part 2 is concerned with corpuscular radiation, and includes the absorption of emanation and some controversial therapeutic methods, with a short appendix on neutrons. Part 3 deals with ultraviolet light—the changes it produces in the skin, its antirachitic effect and its use in the treatment of tuberculosis. Among other matter in part 4 is a chapter on diseases caused by light, is interesting, but the possible carcinogenic effect of bright sunlight might have received more attention. In the fifth part some general principles of radiation biology and therapy are considered and this provides a convenient summary of opinion on the method of action of radiation, radiosensitivity, the time factor and dosage. There is an excellent bibliography and the whole book will be most useful for reference.

Essentials for Final Examinations in Medicine

JOHN DE SWIET, M.D. Lond., M.R.C.P., assistant physician to Staines Emergency Hospital. London: J. and A. Churchill. Pp. 168. 7*s.* 6*d.*

THIS is a small volume of précis articles arranged under 93 headings in alphabetical order. They are practically specimen answers to "spotted" questions, largely compiled from standard textbooks and recent monographs. The style is succinct and clear; the matter, with occasional exceptions, would be acceptable to orthodox examiners, though some might wish for more emphasis on the relation of anginal pain to effort, and some might wonder how it comes about that "the smaller the dose of zinc protamine insulin the sooner it comes into action." But on the whole the student whose own notes are incomplete will find these useful and reliable for last-minute revision.

ECONOMIC WAR OR "SHOOTING" WAR

PAUL EHRLICH once said that "we must learn to shoot microbes with magic bullets" and his untiring researches did indeed succeed in providing a suitable missile for that elusive, twisting target, the spirochaete.

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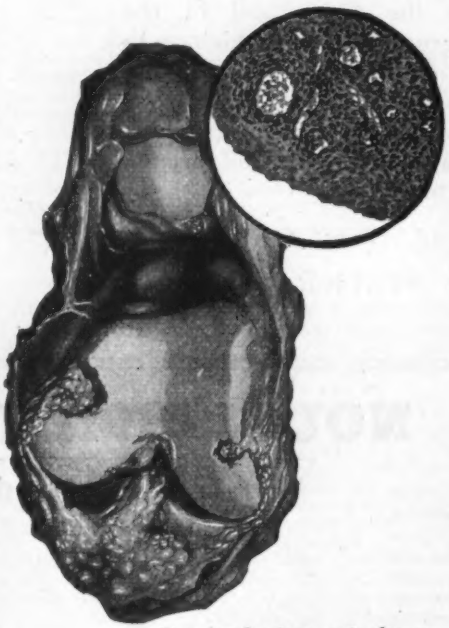

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THE LANCET

LONDON: SATURDAY, NOVEMBER 15, 1941

WHAT'S IN THE NATIONAL WHEATMEAL LOAF?

WHEN the Medical Research Council drew up its second memorandum[1] on national flour in the spring of 1941 it offered the nation something new. Never before had knowledge been sufficient to select with confidence a loaf which would look and taste almost like white bread and yet contain such a large share of the best nourishment of the whole wheat grain. The Medical Research Council's specification was definite, and if it had been adhered to and the new loaf had appeared simultaneously everywhere, uniform in character, attractive in appearance and easy to get, and if, just before and during its appearance, an earnest and urgent propaganda campaign had been undertaken, there can be no doubt that it would have found wide acceptance. At least all those people who could be reached through their sense of duty to promote their own health and that of others, or to protect the lives of our merchant seamen, would have responded. Many others would have tried the loaf through curiosity and if the loaf had been palatable would have continued to do a duty found not so unpleasant after all.

Unfortunately, the national wheatmeal loaf was not launched in this way. The millers did not produce the flour to any uniform specification, the bakers often baked it badly or not at all, and many retailers did not stock it and showed no interest when asked about it. The Government propaganda was feeble. Finally, on Aug. 27, 1941, the final blow was struck in one of the Statutory Rules and Orders of the Ministry of Food,[2] which gave the following definition.

> "National wheatmeal" means flour produced in the United Kingdom and consisting of 85% by weight of any of the products of the milling of clean wheat, provided that the remaining 15% of the products of that milling are the substances commercially known as fine wheatfeed and straight run bran; and includes any such flour to which has been added any substance authorised by the Minister to be an ingredient of national wheatmeal."

This definition makes no fine distinction as to selection of the most nutritious parts of the grain, and permits 85% national wheatmeal to consist of white flour with added bran. A glance at the interior of the national wheatmeal loaf as baked in some parts of the country suggests that this is indeed the case. The Medical Research Council, in making their definition of 85% national wheatmeal, chose two special safeguards; the flour was to contain not less than one International Unit of vitamin B per gramme and less than 0·9% of fibre. These two criteria neatly set the limits within which the composition of the flour should fall. The first would prevent the flour being too white (too much refined); the second would exclude the coarse bran and prevent the flour from being too dark and containing too much roughage. This second criterion is the one which safeguards the interests of those who prefer the taste of white bread. It is the bran which contributes the high fibre content, it is the bran whose taste is disliked by those who do not care for brown bread, and it is the bran which imparts the unpopular dark colour and coarse texture. Investigation of the national wheatmeal loaf, as now supplied, has shown that the loaf which is disliked is the one of high fibre content. This loaf is becoming more and more the rule; the national wheatmeal loaf is steadily deteriorating and consequently disappearing. The flour in such national wheatmeal loaves of poor quality is said mostly to come from the few large milling concerns whose representatives claimed that the Medical Research Council's specification for 85% flour would put too great a strain on the small miller. Actually, it seems, the small millers, whose voices are not heard, have made a more loyal effort in the country's interests.

In this conflict between the national and individual interests the millers have thus won the day, and a golden opportunity of furthering the health of the people has been lost. The situation of the national wheatmeal loaf after this defeat is now strategically bad but is it irremediable? A good loaf, made to a strict specification and supported by wise propaganda, might still achieve victory.

1. *Lancet*, 1941, 1, 703.
2. Emergency Powers (Defence) Order, 1941, No. 1291, Food (Flour). H.M. Stationery Office. 3*d*.

T.N.T.

THE internal combustion engine and the high explosive, trinitrotoluene, belong to the category of doubtful benefits which scientific progress has given to the world, and the doubt is more than doubled when they come together in a bombing aeroplane. T.N.T. has gained great popularity as an explosive since it was first made in the laboratory by HEPP in 1880 and since its adoption by the German military authorities in 1902. As a blasting powder in peace-time it was used for its excellent properties of high stability as an explosive and low toxicity for human beings. It can be hammered or turned in a lathe without exploding, and from the pharmacological point of view the toxic and lethal doses are relatively enormous. Indeed PROSSER WHITE[1] in 1901 showed that dinitrobenzene was more poisonous to animals than trinitrotoluene, and he said that in some factories T.N.T. had been substituted for D.N.B. with great advantage to the health of the workers. This was the attitude towards T.N.T. up to the onset of the war of 1914–18, and paradoxically the "safe" properties of the explosive, because reliance was placed on them, led to a great deal of mischief in the form of poisonings and accidental explosions. In the peace-time manufacture and handling of T.N.T. little trouble is experienced but when war comes the demand for the explosive is enormous, many more workers are exposed to it, longer hours are worked, production is speeded up, new factories are built or adapted, and engineering and managerial skill becomes diluted. It is then that poisoning from T.N.T. becomes a major problem, as was well shown by our experience during the last war.

The first fatality attributed to poisoning by T.N.T. was in February, 1915, and LEGGE[2] describes how at the autopsy he was struck by the jaundice of the sclerotics and skin resembling that seen in poisoning by

1. Prosser White, R. *Lancet*, 1901, 2, 582, 769.
2. Legge, T. M. Annual Report of Chief Inspector of Factories for 1917, p. 21.

aeroplane dope or tetrachlorethane. In the summer of 1915 other cases occurred and two more deaths were reported. Energetic steps were taken to investigate the problem and to prevent cases of poisoning. The Medical Research Committee was asked to inquire into the toxicology of T.N.T. and in the meantime LEGGE had warned the factories, on the analogy of experience with the nitro derivatives of benzene, that T.N.T. might be absorbed through the skin or be inhaled as dust or fume, and he recommended that precautions be taken against both these modes of entry. Towards the end of 1915 it became necessary to obtain more information about the prevalence of T.N.T. poisoning and toxic jaundice became notifiable under section 73 of the Factory and Workshop Act, 1901, although T.N.T. also sets up dermatitis, gastric symptoms, cyanosis (methæmoglobinæmia) and aplastic anæmia. LEGGE explained that the jaundice of T.N.T. poisoning was chosen because when a statutory notification of an industrial disease has to be made the doctor and the factory occupier usually need a definite symptom or sign to guide them. An attempt to notify all the forms of T.N.T. poisoning would mean that the figures would include nearly every T.N.T. worker seeking medical treatment for any complaint. The order for notification came into force on Jan. 1, 1916, and 181 cases of toxic jaundice with 52 deaths were notified in that year, whereas in 1917 there were 189 cases with 44 deaths. The greatest number of cases were observed towards the end of 1916 and the beginning of 1917, after which the incidence of toxic jaundice and deaths fell rapidly although many more workers were engaged in the manufacture of T.N.T. and in the shell-filling factories. Writing in war-time LEGGE could not give the precise numbers of workers exposed to the risk of poisoning but he indicated that there were well over 50,000 so employed. In the meantime MOORE,[3] with his colleagues WEBSTER and WYON, had been carrying out in the laboratory and the field a brilliant series of researches which established the fact that T.N.T. made its way into the body more often through the skin than by way of the lung passages or the alimentary tract. Early in the inquiry WEBSTER[4] evolved a chemical method of determining the excretion of altered T.N.T. in the urine (a modification of the test by INGHAM[5] was published in our columns last week), and armed with this the investigators were able to test the efficacy of the preventive measures which were put into force. They also showed that the skins of different individuals had varying capacities for absorbing T.N.T. and letting it through into the blood-stream, and that workers who developed dermatitis rarely showed constitutional symptoms. The colour reaction obtained by Webster's urine test is due not to T.N.T. itself but to a reduction product (2 : 6 dinitro : 4 : hydroxylaminotoluene); on excretion in the urine this is conjugated with glycuronic acid, which shares with the sulphonic esters the task of removing from the body in innocuous form a large number of poisonous substances which are either formed autogenously in the body or are introduced from without. Herbivorous animals show a greater tolerance than carnivora for T.N.T. and man with his mixed diet stands in an intermediate position. Some diets yield more glycuronates or glycuronic esters than others and it seemed important to provide for all workers on toxic nitro compounds a diet with a high yield of these substances—for example, fresh vegetables and fruit. Some resemblance was noted between certain manifestations of T.N.T. poisoning, such as purpura hæmorrhagica, and those of scurvy. It may be noted that in war-time supplies of fresh fruit are restricted.

It would be interesting to know how many cases of T.N.T. poisoning there have been during the present war but no figures were given in the report of the Chief Inspector of Factories for 1940.[6] Last week we published a description by R. M. EVANS[7] of seven cases of toxic jaundice due to T.N.T. in a shell-filling factory. Two of the cases ended fatally and in one of these the patient, who died from acute liver atrophy, had been in contact with explosives for only 3 weeks before the onset of the illness. The second death was from aplastic anæmia which came on 9 weeks after an attack of toxic jaundice had abated. HILTON and SWANSTON[8] in an article on the general aspects of poisoning by tetryl and trinitrotoluene mentioned that they have seen 3 (presumably recent) fatal cases of aplastic anæmia in workers exposed to T.N.T. But we do not know whether the position as regards T.N.T. poisoning is better or worse than it was during the last war. Many are asking, as EDWARD VII asked about tuberculosis—"If preventable, why not prevented?" But the principles of prevention of poisoning by T.N.T. are well known and there can be little doubt that as far as is humanly possible they are being applied. In T.N.T. factories all workers are under close medical supervision and the engineers coöperate to control the dust and fume. But as BRIDGE[9] points out there is still no explanation why some people after a short period of exposure are poisoned by T.N.T. while others working under the same conditions escape. ROBERTS,[10] in urging the need for selection of workers, says that those who are susceptible to T.N.T. may not be protected by even the most satisfactory working conditions and most careful supervision. He suggests that no-one under the age of 19 and no woman weighing less than 105 lb. should be allowed to come in contact with T.N.T., and that anyone with sweaty hands, a history of jaundice or the yellow sclerotics often seen in constipated people should be rejected. He also urges attention to the workers' habits of personal cleanliness—whether they sleep in underclothing that they wear at work, whether they bite their nails, or have long tapering ones. MOORE made some suggestions about the part played in determining susceptibility by both diet and permeability of the skin, which can be tested by rubbing in a measured quantity of T.N.T. and assessing by Webster's test the amount absorbed and excreted in the urine. But, until a really reliable method of pre-employment selection is found whereby susceptible individuals can be kept away from T.N.T., cases of poisoning are to be expected in small numbers even if all other methods of prevention are rigorously applied. Meanwhile workers must not be sacrificed to the exigencies of output by being kept in the workrooms longer than is reasonable.

3. Moore, B. *Spec. Rep. Ser. med. Res. Comm.* 1917, No. 11.
4. Webster, T. A. *Lancet*, 1916, **2**, 1029.
5. Ingham, J. *Ibid*, 1941, **2**, 554.
6. H.M. Stationery Office. Pp. 24. 4*d*.
7. Evans, R. M. *Lancet*, 1941, **2**, 552.
8. Hilton, J. and Swanston, C. N. *Brit. med. J.* 1941, **2**, 509.
9. Bridge, J. C. Annual Report of Chief Inspector of Factories for 1940, p. 23.
10. Roberts, H. M. *Brit. med. J.* 1941, **2**, 647.

TRAUMATIC DEAFNESS

WHEN man learnt to make noises louder than nature intended his ears to bear traumatic deafness must have made its appearance, and gunfire deafness must have come in with guns, though the first cases reported, according to GOLDSTEIN, seem to have been those of SOLOMON ALBERTI of Nuremburg in 1591, when guns had been in use for some 200 years. The industrial revolution, and particularly the development of heavy industries during the present century, has added another form of traumatic deafness. Long exposure to the louder industrial noises produces temporary, or sometimes permanent, deafness in certain people—so-called boilermaker's deafness. Between 1915 and 1930 most aircraft were of the open-cockpit type and the pilot and passengers were exposed to the noise of the engine and air-screw and also the wind-rush. In this period otologists in various countries discussed a form of deafness which aviators developed as an occupational disease. All agreed that temporary deafness was almost the rule and that permanent deafness was reasonably common. The type of deafness was identical with that found in other noisy occupations, and in fact all forms of traumatic deafness where there is no gross demonstrable lesion of the drum, ossicles or bone are of a similar type, varying only in severity. POLITZER [2] described traumatic deafness as being of the nerve type, and this view is supported by KERRISON.[3] The differentiation from other forms of nerve deafness was first made by BUNCH [4] in an analysis of a number of audiometric tests. In senile deafness there is little loss of auditory acuity for tones up to about 512 double cycles, but thereafter the acuity diminishes almost proportionately to the rise in frequency. Toxic deafness follows a somewhat similar, but usually more intense, pattern. BUNCH found that the hearing in cases of traumatic deafness is fairly normal for frequencies up to 2048, after which there is an abrupt fall in the curve, maximal at 4096 double variations and improving at higher frequencies. A similar finding was recorded by FOWLER,[5] who also formulated the generalisation that the medium-high frequencies are especially sensitive to insult from trauma or toxins. These observations indicate a lesion of the second half of the basal whorl of the cochlea, and confirmation came from an investigation of the microscopic anatomy by CROWE, GUILD and POLVOGT,[6] who discovered that there was atrophy of the organ of Corti at a level above the last 2 mm. of the basal turn. This region corresponds fairly exactly to the opening of the oval window and to the promontory on the inner wall of the middle ear. In other words, that part of the cochlea nearest the external world and first receiving the auditory impulses suffers most damage.

In attempting to avoid deafness due to noise, blocking the external meatus has been advised and used for years. For the less intense and prolonged noises the method is reasonably successful. DICKSON and EWING [7] have recently investigated various methods of protecting personnel engaged in flying modern aircraft or handling them on the ground. The noise with which they were concerned is very loud, lasts for a considerable time and is subject to brief impulsive intensification. In addition to protecting against these peculiar noise properties, the method sought had to permit the reception of intelligible speech. As might be expected, the solution of so paradoxical a problem was not wholly satisfactory. Two forms of protective appliance were investigated —ear-plugs of various materials, and complete helmets. The chief function of the ear-plugs was to reduce air transmission through the middle ear, and of the helmets to insulate the bones of the skull and reduce conduction through the bony capsule. Combination was more effective than either method alone but proved unpractical because of the gross interference with the reception of speech. With both methods there was less protection against noise in the lower than in the higher frequencies, but it has already been shown that the deafness occurs in the medium-high range where it causes the greatest handicap. Both plugs and helmet successfully delayed the onset of aural fatigue but did not abolish it, and this is about as far as it is yet possible to go. However, enough has been discovered to indicate that something can be done at least to mitigate one of the many disabilities resulting from war. More still might be done if these cases were followed up carefully. It would not be difficult to keep men deafened by aircraft noise under observation, to have audiograms done regularly, and to seize any opportunity that fatal accidents offered to secure the temporal bones. A few autopsy specimens, backed by a full history and investigation, might teach us much of the pathology of traumatic deafness and show the way to complete prophylaxis.

1. Goldstein, M. A. Problems of the Deaf, St. Louis, 1933.
2. Politzer, A. Diseases of the Ear, Philadelphia, 1926.
3. Kerrison, P. D. Diseases of the Ear, Philadelphia, 1930.
4. Bunch, C. C. *Arch. Otolaryng., Chicago*, 1929, **9**, 625; *Laryngoscope, St. Louis*, 1937, **47**, 615.
5. Fowler, E. P. *Trans. Amer. otol. Soc.* 1929, **19**, 182.
6. Crowe, S. J., Guild, S. R. and Polvogt, L. M. *Bull. Johns Hopk. Hosp.* 1934, **54**, 315.
7. Dickson, E. D. D. and Ewing, A. W. G. *J. Laryng.* 1941, **56**, 225.

MORE ABOUT PHAGE

THE principle of setting a thief to catch a thief seemed likely to be applicable in therapeutics when first F. W. TWORT and then D'HERELLE found twenty-five years ago that cultures of bacteria in the test-tube could mysteriously disappear and when subsequent work showed that many bacteria, pathogenic and non-pathogenic, were the prey of the propagable lytic substance now known as bacteriophage. The nature of this substance is still in dispute. Most bacteriologists adhere to the view that phage belongs to the virus family, and that there is a multiplicity of phage-viruses each specific for its own bacterial host rather than one omnivorous phage as D'HERELLE maintained. Others follow BORDET in regarding phage as an autocatalytic enzyme derived from the bacterium itself, while others, like LWOW, believe in a gene origin of phage. Whatever its nature, the therapeutist soon found that the promised panacea had once again eluded him, for in both experimental and clinical infections phage proved disappointing. The main reason for its failure was its inactivation by any protein or colloid with which it came in contact, although the use of non-specific phage-lysates of weak potency was probably a contributory factor. Even in the test-tube a sufficient concentration of phage is required to lyse a bacterial culture. EATON and BAYNE-JONES [1] concluded in

1. Eaton, M. D. and Bayne-Jones, S. *J. Amer. med. Ass.* 1934, **103**, 1769, 1847, 1934.

1934 that the field of phage-therapy was limited to surface infections, whether of skin or mucous membrane, such as pyodermias, urinary and intestinal infections, and both in America and on the Continent phage still enjoys a certain popularity in the treatment of such conditions as boils, cystitis and dysentery. The work done since 1934 has been critically reviewed by KRUEGER and SCRIBNER,[2] who point out that there may be a variety of reasons other than direct lytic action on the pathogen for the apparently beneficial action of phage in both local and systemic infections. For example, intravenous injections of phage-lysates may, in virtue of their content of broken-down protein, stimulate a leucocytosis or produce the condition of protein shock which often helps to overcome a subacute infection. Phage-lysate certainly stimulates the formation of specific antibody to the infecting organism, as GREENWOOD, TOPLEY and their co-workers[3] demonstrated in mouse-typhoid. Sometimes, as in the case of the staphylococcus, the phage denatures the bacterial protein, but any preformed toxin would still be present. More specifically, phage might attack the more susceptible infecting organisms, leaving a less susceptible but also less virulent variant to be overcome by the host's tissue, but GREENWOOD and TOPLEY found when using phage in attempts to control epidemics of mouse-typhoid that a natural variation of this kind hardly ever occurred. Applied locally, as in the treatment of boils, the beneficial effect of phage may again be due to a non-specific stimulus of the host's defensive mechanism, for local applications of bacteria-free nutrient broth have been found to be equally effective.

When these collateral effects are discounted, bacteriophage is still found to act specifically on certain bacterial infections, provided it can be applied in sufficient concentration. The diseases which hold out most promise of success are the local bowel infections—dysentery and cholera—and it is particularly important just now to know what phage can do for these. A great deal of work on the prevention and treatment of cholera with phage has been done in India. MORISON[4] has treated wells in certain districts of Assam with anticholera phage while other districts served as controls, and his results seem promising. In treatment MORISON's fatality-rates in two large series were 22·6 and 21% for treated cases and 55·6 and 70% for controls, with a greatly diminished secondary case-rate in the families of treated cases. PASRICHA and his colleagues,[5] in a carefully controlled series of hospital cases, recorded only a slight difference in the fatality of phage-treated and untreated cholera, but among bacteriologically positive patients the fatality in the treated group was only 8·3% compared with 20·6% for the untreated. Thus, the evidence is favourable to the continued use of phage both in the prevention and treatment of cholera. In dysentery the position is more controversial. Enthusiasts like COMPTON[6] recommend phage-therapy without reservation and claim dramatic results. From Germany[7] comes a report of the treatment of 32 soldiers suffering from a mild Flexner infection with disappearance of symptoms in 2–4 days: 10 c.cm. of a dysentery polyphage was given in coffee after a preliminary dose of 0·5–1 g. of soda bicarbonate to protect the phage against the destructive action of the gastric juice. Others have claimed that dysentery phage can be used as a prophylactic in local outbreaks of the infection, and the war in the Middle East should provide an opportunity for testing the value of phage in dysentery under controlled conditions. But potent and specific lysates must be used if any success is to be obtained.

Phage has been used extensively in America for the treatment of local suppuration, and indeed ALBEE believed that the healing of chronic osteomyelitis by the Winnett Orr technique is largely due to spontaneous or implanted phage-activity. Phage seems to have yielded good results in peritonitis and intestinal perforation but there it is likely to be superseded by the local application of sulphonamides. In systemic infections it has been applied principally to the treatment of staphylococcal septicæmia. In a recent series LONGACRE, ZAYTZEFF-JERN and MELENEY[8] divided their cases into those treated with phage before and after 1936, when a more potent phage was introduced. In the first group of 15 cases the fatality was 73·3%; in the second group of 21 cases it was 28·5%. They gave frequent and increasing doses intravenously until the patient was getting 50 c.cm. per day, and claimed that phage of high potency, given early and in adequate dosage, offers a good prognosis in this serious infection. KRUEGER and SCRIBNER are doubtful if the benefit reported in septicæmic conditions can be due to a direct lytic action on the organisms in the blood-stream or tissues; yet the experimental work of ASHESHOV, WILSON and TOPLEY[9] showed that antityphoid phage injected intravenously could inhibit infection in mice given a lethal dose of the organism intraperitoneally, though it did not cure an established infection. Other workers have confirmed these experimental results, which demonstrate that phage injected parenterally is not wholly inactivated by the host's tissues. Thus, although phage-therapy is for the time being overshadowed by chemotherapy, it may yet prove a useful weapon.

2. Krueger, A. P. and Scribner, E. J. *Ibid*, 1941, **116**, 2160, 2269.
3. Greenwood, M., Hill, A. B., Topley, W. W. C. and Wilson, J. *Spec. Rep. Ser. med. Res. Coun., Lond.*, 1936, no. 109.
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6. Compton, A. *Brit. med. J.* Aug. 23, 1941, p. 280.
7. Guthof, O. *Disch. med. Wschr.* April 4, 1941, p. 375.
8. Longacre, A. B., Zaytzeff-Jern, H. and Meleney, F. L. *Surg. Gynec. Obstet.* 1940, **70**, 1.
9. Asheshov, I. N., Wilson, J. and Topley, W. W. C. *Lancet*, 1937, **1**, 319.

GERMAN VITAL STATISTICS.—An official bulletin gives the number of marriages in Germany in 1940 as 715,400 against 944,331 in 1939. The number of live births in 1940 was 1,644,752 and the birth-rate per 1000 inhabitants 20·4. In the territory of the old Reich the birth-rate dropped to 20, the balance being made up by Austria, Sudetenland, Memel and Danzig. It is estimated that as a result of the war 150,000 fewer children were born in 1940. The number of deaths for 1940 was 36,450 more than in 1939. The death-rate increased by 0·4 per thousand to 15. This increase is attributed to the cold spell in 1940. The most important causes of death were cardiac diseases 19·6%, cancer 16%, cerebral apoplexy 10·2%, pneumonia 9%, tuberculosis 6·8%. The increase in deaths from tuberculosis—2000 more than in 1939—is also ascribed to the cold spell. Infantile deaths were roughly 7500 more than in 1939. The death rate per 1000 live births was 65. The net increase in population amounted to roughly 600,000. Some figures for the first quarter of the year 1941 have already been cited (*Lancet*, Aug. 23, p. 235).

Annotations

TOWN ⟷ COUNTRY

THE evacuation of London school-children is now two ears old, and in the balance-sheet presented to the ducation committee of the London County Council on ov. 5 the chairman was able to show a reasonable rofit-and-loss account. What the children have missed n the way of formal education they have gained in ental and physical vigour and a new breadth of outlook. he constant ebb and flow of children and teachers ecessitates the frequent reorganisation of classes, and he scarcity of new entrants makes it difficult to maintain eparate departments for juniors, seniors and infants. ut if classes have a wider range, they are smaller than n London and there is more scope for individual study. t school the children may find their quarters cramped nd the sanitary arrangements inadequate according to ondon standards, but good food, early bedtime and resh air have improved their health, and the town hildren have a better attendance record than the local hildren and show more resistance to epidemics. If there s a shortage of school books and equipment, nature tudy and practical geography are attractive new lessons; f the gym, playground and swimming baths are small r non-existent, and if equipment for domestic science, rt and crafts is lacking, the children have found new ploys such as milking, bee-keeping, poultry-keeping and, bove all, gardening. To many it was news that peas, eans and cabbages have a history that goes beyond the reengrocer in Deptford High Street, but now the boy om Bermondsey brags about his "sprarts" and makes is plot an economic as well as a horticultural success.

No-one can read the report without feeling admiration or the London teachers, who now often look after their oung charges in and out of school hours and during the olidays. The closer relationship between teachers and hildren has been one of the gains of evacuation. The eachers are often leading rather lonely lives, isolated from ooks, professional contacts and home ties; yet it is due o their enterprise that the children have sometimes been ble to contribute to the life of the community, and school oncerts and displays of handiwork have been warmly elcomed by the country dwellers. But the country does ot seem to have made many lasting converts. When he rest of their family remains in town, it is only natural hat the children should return when they leave school, nd in an inquiry among 1500 "leavers" less than a uarter remained in the reception area, and of these very ew were taking up farming or agricultural work.

THE STICKINESS OF PLATELETS

IT is a classical observation that blood-platelets and hite cells collect at the point of injury of a blood-vessel nd there form a thrombus; Osler remarked on the way latelets stick to foreign particles. But although methods have been described for estimating the adhesive-ess of white cells, no-one has tried to measure this roperty in platelets. Payling Wright[1] has devised an ingenious method of following the changes in the sticki-ess of blood-platelets that are caused by the use of arious anticoagulants, and incidentally she has sug-ested an explanation of the disappearance of platelets in tored blood. Specially shaped glass bulbs were used hich had carefully ground apertures at either side; hese apertures were sealed with coverslips held in place with soft paraffin. Blood was collected in an oiled syringe, mixed with dry anticoagulant in a waxed beaker, and then transferred to the glass bulbs which were steadily rotated by a motor. For control, some of the blood was put into a bulb coated on the inside with soft paraffin. The platelets were counted by a standard method before the blood was put into the bulbs and then at regular intervals afterwards. Finally the coverslips were detached, stained by Leishman's method and examined. It was found that after 80 minutes the platelet count had fallen to between 60 and 20% of the original count; the final figure depended on the anti-coagulant used, but still more on the concentration of the anticoagulant. Oxalate, heparin, chlorazol pink, and chlorazol blue were tried. With a concentration that would just prevent clotting, the platelet count after 80 minutes' rotation fell to 20–25% of the initial count with all these anticoagulants; but when concentrations of eight or more times minimal were used the final count in oxalated blood was about 60% of original and about 45% with the other anticoagulants. In the control bulbs there was only a slight fall in the platelet count. When the stained coverslips were examined, the missing platelets were found sticking to the glass, and it was noticed that at the higher anticoagulant concentrations the platelets tended to adhere only to the glass and not to each other. Payling Wright concludes that anti-coagulants reduce the stickness of platelets, possibly by reducing fibrin formation on their surfaces. The disappearance of platelets in stored blood is due to their adherence to the walls of the storage bottles and not to disintegration, for had this happened clotting might well have been expected when the anticoagulant concentration was minimal and the fall of the platelet count large; but no clotting occurred. This technique can clearly be extended to pathological problems. Are the blood-platelets less sticky in purpuras? Can "thromb-asthenia" be demonstrated? Will the answers help us to decide between the orthodox school who think that the stickiness of blood-platelets assists the actual plugging of injured blood-vessels and those who hold that they only help to initiate clotting in the shed blood.[2] This method might also be used to seek materials, possibly plastics like Perspex, that platelets will not stick to and could be used for the collection of platelet-containing blood.

1. Payling Wright, H. *J. Path. Bact.* 1941, **53**, 255.

TOO MUCH OF A GOOD THING

NATURE has been none too bountiful with her supplies of the vitamins, as the widespread incidence of deficiency diseases shows. The possibility of overdosage, therefore, hardly arose before the interference of man led to the detection, isolation and finally synthesis of several of their number. After the synthesis of calciferol by the irradiation of ergosterol, the too energetic exhibition of this substance to infants and children led to several instances of undue calcification and occasional death.[3,4] Hypervitaminosis A has not yet been described in humans, although it can be produced experimentally in rats.[5] Overdosage is more readily to be expected with these fat-soluble vitamins, which are not easily eliminated by the body, than with the water-soluble factors, excess of which is readily excreted in the urine. Nevertheless, a large dose of a water-soluble vitamin might cause for a short time a high concentration in the blood and so possibly lead to untoward symptoms. This, for example, is true of nicotinic acid. Doses of more than 50 mg. by mouth or 10 mg. intravenously may produce flushing and irritation of the skin, and occasionally gastrointestinal symptoms.[6] These effects are transitory; the concentration of the vitamin in the blood rapidly falls as the excess, which is not metabolised or stored, is excreted by the kidneys. Whether large doses of the other water-soluble factors produce undesirable reactions is not certain. It has been suggested that intense treatment with vitamin B_1 may give rise to symptoms akin to those of herpes zoster—intense irritation of the skin and a burning pain in peripheral nerve areas.[7]

2. See *Lancet*, May 3, 1941, p. 574.
3. Hess, A. F., Lewis, J. M., and Rivkin, H. *J. Amer. med. Ass.* 1930, **94**, 1885.
4. Harris, L. J. *Lancet*, 1932, **1**, 1031.
5. Takahashi, Nakamiya, Kawakimi and Kitasato, *Sci. Pap. Inst. phys. chem. Res* 1925, **3**, 81.
6. E.g., Spies, T. D., Bean, W. B. and Stone, R. E. *J. Amer. med. A* 1938, **111**, 584.
7. Steinberg, C. L. *Amer. J. digest. Dis.* 1938, **5**, 680.

In all these instances excessive intake produces—or is said to produce—changes which are related to the known action of the factor concerned as indicated by the effects seen in deficiency. This was first shown with hypervitaminosis D, which gave rise to an increase in the blood level of phosphate and calcium with consequent calcification.[4] Excess of nicotinic acid affects the skin and occasionally the gastrointestinal tract, and excess of vitamin B_1 is reported to affect the nerves. A novel aspect of hypervitaminosis, however, has recently been studied by Loewenthal of Basle.[8] He suggests that large amounts of ascorbic acid, which are excreted by the kidney, might produce changes in the urine conducive to the formation of urinary calculi. Loewenthal ingested 1 or 2 g. of the vitamin daily for five weeks and carried out several types of investigation—some rather unusual—on the urine before and during this period. The effect of the vitamin was to produce an increase in the titratable acidity of the urine, an increase in the turbidity and a change in the gold-sol reaction (a test usually applied to the C.S.F.). He does not profess to be able to explain the exact nature of these last two changes but interprets them simply as indicating an alteration in the "protective colloids" of the urine. This, together with the increased acidity, are assumed to imply a greater tendency to the formation of urinary calculi. These tentative conclusions will require a great deal of confirmation and elaboration. But even if true, they will certainly not deter us from the appropriate and adequate treatment of suspected deficiency of vitamin C. The daily requirements of the vitamin are probably about 50 mg. and even a case of severe scurvy will be cured by the administration of 1 g. daily for a week or two. Doses such as those taken by Loewenthal are thus rarely if ever required. Moreover, the fact that unnecessarily large overdoses of vitamin D produce toxic symptoms has not interfered with the cure or prevention of rickets by the intelligent use of this substance.

The danger of hypervitaminosis in ordinary conditions of therapy or prophylaxis is often exaggerated, but its existence may at least serve the useful purpose of directing attention to the quantitative aspect of vitamin dosage. There is a tendency to order a convenient preparation without thinking of the amount of the vitamin really desired. The possibility of overdosage, and incidentally a great deal of waste of precious nutritional material, will be avoided when vitamins are prescribed in units or milligrammes or in human "daily shares" and not as so many capsules or tablets.

MANIFESTATIONS OF ENDEMIC FLUOROSIS

SURVEYS in America [9] and in England [10] have shown that in children the mottled enamel of mild endemic fluorosis is associated with a greater than average resistance to dental caries, and that the toxic action of fluorine tends to affect those whose general nutrition is poor. In other parts of the body fluorine may exert an indirect action. Young and his colleagues [11] pointed out that in the ætiology of endemic goitre the absolute iodine content of the water and soil is not the only factor and that something else determines the availability of the iodine to meet human and animal needs. In at least one area of this country, among people living under conditions of low iodine intake Wilson [10] has established a relationship between the distribution of goitre, of fluorine in rock and of mottled enamel. In the locomotor system fluorosis especially attacks tissues rich in calcium. Roholm [12] described the pathological calcification of tendons, ligaments and fasciæ, and the formation of osteophytes among cryolite workers absorbing large amounts of fluorine. In endemic human fluorosis bone changes were first detected by Shortt and others [13] among communities in South India, and subsequently Pundit and his colleagues,[14] by comparative dietary surveys among these same people, showed that the incidence of bone deformity bore a definite relation to the economic and nutritional state of the communities concerned, indicating again that the toxicity of fluorine is made more evident by a "poor" diet. Recently Ockerse [15] in South Africa has described bone changes among villagers in the Pretoria district using borehole water containing over 11 parts per million of fluorine. Clinical symptoms include stiffness of the spine in the lumbar, thoracic and cervical regions, and pain and stiffness around the joints of the arms and legs and lumbar regions. The radiograms of an advanced case show ossification with increasing density of bone and calcification of the lumbar and thoracic vertebræ and attachments; osteophytic outgrowths and periosteal deposits are also present along the radius and ulna and around the elbow-joint and margins of the ribs. The clinical picture is similar to that of the most severe cases in South India. Fluorine, then, has a claim to be one of the trace elements necessary for nutrition, but its intake must be carefully limited and balanced with adequate iodine and the other factors influencing ossification. Unfortunately we have a long way to go before we can decide what the optimum intake of fluorine is and can ensure that everyone gets it.

STETHOSCOPES OLD AND NEW

SINCE that day in 1816 when Laennec took a quire of paper, rolled it up to form a tube and applied it to the chest of a corpulent young woman, the art of auscultation has been developed to a fine degree. Although "immediate" auscultation seems to have been practised by Hippocrates and Harvey, medical men were slow to appreciate the significance of the heart sounds. Indeed Parisanus (1663), a physician of Venice, rejected Harvey's observations with the words "Nor we, poor deafs, nor any other doctor in Venice can hear them, but happy is he who can hear them in London." The great Corvisart, nearly two hundred years later, referring to the heart sounds, wrote "I have never had an opportunity, I repeat it, of ascertaining the unquestionably rare observations; I have barely heard these strokes by applying my ear close to the patient's chest." Both statements, in their obtuseness, recall Sir James Mackenzie's words on another aspect of cardiac examination. "Indeed I am doubtful," he wrote in 1920, "if an X-ray examination of the heart has ever thrown the slightest light on any cardiac condition." From the roll of paper to the perforated wooden cylinder was Laennec's next step, while Piorry's modifications and his addition of ear piece and chest piece in 1828 resulted in what is essentially the monaural stethoscope of recent times. Williams probably described the first binaural model about 1843 while Cammann replaced the lead tubes by flexible ones in 1855. Thus, briefly, was evolved the modern binaural stethoscope.

The chest piece in all these models was funnel or trumpet shaped. In the phonendoscope, invented by Bianchi in 1894, a diaphragm chest piece with a rigid membrane was first used. The combined bell and diaphragm chest piece of the latest models seem satisfactorily to cover the acoustic ranges necessary for clinical examination of the heart and lungs. In a recent study of the laws governing auscultation Rappaport and Sprague [16] of Boston point out that the bell chest piece when applied to the patient's chest functions in reality as a diaphragm chest piece. The skin enclosed by the lip of the bell acts as a diaphragm, while the subcutaneous

8. Loewenthal, M. *Schweiz. med. Wschr.* 1941, **71**, 761.
9. Dean, H. T., Jay, P., Arnold, F. A. Jun. and Elvove, E. *Publ. Hlth Rep. Wash.* 1941, **56**, 761.
10. Wilson, D. C. *Lancet*, 1941, **1**, 211, 375.
11. *Spec. Rep Ser. med. Res. Coun. Lond.* No. 217, 1936.
12. Roholm, K. Fluorine Intoxication, London, 1937.
13. Shortt, H. E., McRobert, G. R., Barnard, T. W. and Nayar, A. S. M. *Ind. J. med. Res.* 1937, **25**, 553.
14. Pundit, C. G., Raghavachari, T. N. S., Subba Rao, D. and Krishnamurti, V. *Ibid*, 1940, **28**, 559.
15. Ockerse, T. *S. Afr. med. J.* 1941, **15**, 261.
16. Rappaport, M. B. and Sprague, H. B. *Amer. Heart J.* 1941, **21**, 257.

tissue becomes a damping medium. The larger the diameter of the bell chest piece the better its response to low-pitched sounds. This is accomplished at the expense of high-frequency components. By increasing the pressure of the bell chest piece on the patient's chest one is able to increase the natural period of the skin diaphragm and thereby attentuate the lower-pitched components. Higher-pitched sounds are then accentuated as a result of the decreased masking effect. Thus loud first and second sounds, and a loud systolic murmur of fairly low pitch are damped down, while a high-pitched diastolic murmur will stand out better. When the pressure on the chest piece is reduced, low-pitched murmurs, third heart sounds and gallop rhythms may be elicited more readily. The diaphragm type of chest piece is especially useful in detecting faint, high-pitched sounds, such as the diastolic murmur of aortic incompetence and the "bronchial" respiratory sounds. If the diaphragm is too thick, however, there is a general reduction of sound intensity. Rappaport and Sprague found that the optimum diameter of the bell chest piece is 1 in. and that of a bakelite diaphragm 1½ in.; the thickness of the latter should be about 0·015 in. The smaller the diameter of the bell the higher the pitch of the sounds. They think that the bell should not be considered primarily as an accumulator but rather as a microphone or telephone receiver. Finally, as many students may have suspected when they began clinical work, they find the length and calibre of the rubber tubing important. They show that the pressure variations at the ear, produced by the motion of the skin or bakelite diaphragm, are inversely proportional to the internal volume of the stethoscope. It follows, therefore, that the tubing should be as short as possible and the calibre as small as possible. The wall of the tubing should be sufficiently rigid to prevent any wall motion, for that would reduce the effective pressure variations transmitted to the observer's ear. Here they differ from Johnston and Kline,[17] but the latter reached their conclusions as a result of experiments on the human cadaver with a mechanical ear.

SWEAT-GLANDS IN THE DOG

ANOTHER illusion has been shattered, though not apparently for the first time. Speed,[18] of Edinburgh, who has taken the trouble to fix pieces of dog skin in formol and make microscopic sections, has found sweat-glands in them. He makes no claim to a special technique; he has simply followed the biblical injunction to seek. From his fairly comprehensive summary of previous literature it appears that others have done the same and have not always been rewarded. Nevertheless, eight investigators are quoted who have described the glands at various times during the last 75 years. They differ in their estimates of incidence and distribution and in the way the glands communicate with the surface. Speed says that in the hairy parts the glands open into dilatations of the hair follicles between the opening of the sebaceous glands and the skin surface. They are numerous on the skin of the lips, head, back, thorax, shoulders and thighs, but few over the abdomen and groin. They are absent on the hairless skin of the muzzle, on the scrotum and on the perinæum. The sweat-glands of the pads of the feet are easily seen because of the absence of the hair follicles, and, unlike the others, are coiled. Thus perishes the fallacy that the dog pants because he cannot sweat over the general surface of his body. Nevertheless, he does pant, and no microtome can strip him of this well-known singularity. Perhaps he keeps a large part of his "evaporation reserve" in the surface of his tongue and upper respiratory tract, in which case his equipment for making use of the latent heat of evaporation of water seems to be more varied than that of man. No doubt other investigators will pursue the matter further to see whether this advantage is shared by breeds other than the half-dozen tested by Speed. It would be interesting to know how effective the sweating is. The fact that no visible moisture appears argues efficient vaporisation. The probability that a relatively stagnant atmosphere saturated with water vapour is enmeshed in the hairs suggests the reverse.

17. Johnston, F. D. and Kline, E. C. *Arch. intern. Med.* 1940, **65**, 328; see *Lancet*, 1940, **1**, 557.
18. Speed, J. G. *Vet. J.* 1941, **97**, 252.

REPAIR OF THE PERINÆUM UNDER LOCAL ANÆSTHESIA

ATTENTION was drawn last week (p. 569) to the use of local anæsthesia in normal pelvic delivery, and in minor obstetric procedures such as episiotomy and the application of low forceps. Local anæsthesia should also have a place in domiciliary midwifery in the suture of perinæal lacerations. Williams[1] points out, very rightly, that all perinæal tears, however trifling, should be sutured immediately after delivery. In the patient's home this means that a second doctor has to be summoned to give an anæsthetic; otherwise the tear is neglected or inadequately united, either without anæsthesia or under anæsthesia administered by the accoucheur himself—a procedure which leads to carelessness in asepsis and lack of proper supervision of the anæsthetic. Local anæsthesia overcomes these difficulties and the technique is simple. No special instruments are necessary and the only requisite is some form of support to control the patient in the lithotomy position. The left lateral position is unsuitable in that it tends to approximate the torn edges of the wound and so mask the extent and complexity of the area of operation. To ensure an optimum position, the patient's coöperation must be obtained and the nervous patient is unsuitable for this type of anæsthesia. An ordinary 10 c.cm. record syringe is used with fine hypodermic and long serum needles. The solution Williams recommends is 1% procaine, without the addition of adrenaline. The skin edges of the tear, deeper structures and muscles are infiltrated generously, but not so as to balloon them unnecessarily. No. 2 non-chromicised or chromicised catgut and a sharp curved cutting needle are recommended: a needle holder is a useful accessory, but not essential. The area of operation is properly isolated with towels and gently swabbed over with an antiseptic solution such as Dettol. The tear is carefully explored to ascertain its extent, but no matter how severe it may be it will be suitable for suture under local anæsthesia. It must not be forgotten that a small skin tear may indicate serious deep vaginal lacerations running high up towards the vaginal vault, hence the importance of a preliminary survey before starting suturing. For inspection a portable headlamp allows the operator to move about freely and does away with the need for an assistant to illuminate the site of operation. When the repair is complete a finger is inserted into the rectum to assess the power of the anal sphincter and the anatomy of the perinæal body; this will also exclude the unlikely possibility of a suture having transfixed the mucous membrane of the rectum. Should this last disaster be found the whole wound must be taken down and resutured, as such a stitch may actually lead to infection and might predispose to a subsequent fistula. Neal Smith[2] has reported on the successful suture of 17 unselected cases of perinæal laceration, ranging from a small first-degree to a serious perinæal tear. Some were hospital and some district cases and all healed by first intention without any complication. The technique used was exactly similar to that of Williams, except that 2% procaine was used instead of 1%. It is probably always an advantage to use more of a weak solution in local infiltration anæsthesia than less of a strong solution, the ideal

1. Williams, B. *Post-grad. med. J.* July, 1941, p. 117.
2. Smith, D. J. N. *J. Obstet. Gynæc.* 1941, **48**, 610.

being ½ or 1% procaine. Smith like Williams urges the importance of early operation and notes that expedition enhances the efficacy of the anæsthesia. The advantages of local anæsthesia for suture of perinæal tears have long been recognised by a few obstetricians, but for some reasons any operation performed under a local or regional anæsthetic tends to be unpopular in this country both in the minds of the lay and the professional concerned. This is an unfortunate attitude that should if possible be overcome. Inhalation anæsthesia in the mother at or after delivery is always fraught with some small risk and this especially in cases complicated by cardiac, pulmonary or other intercurrent diseases, notably toxæmia. In these cases it is much to be recommended that the small extra trouble of using a local anæsthesia be cheerfully undertaken by the operator, who after all is more concerned with the patient's safety than his own time and convenience.

SIR ARTHUR HILL, F.R.S.

THE tragic death from a riding accident on Nov. 3 of Sir Arthur Hill has removed at the age of 66 years one who was still full of vigour and the zest of life. He had been director of the Royal Botanic Gardens at Kew for the past nineteen years where he had succeeded Sir David Prain. He had a keen artistic appreciation of the beauties of the gardens which he did much to preserve and enhance. During his directorship the extensive addition to the herbarium was erected and the north gallery was restored to its original condition. Hill's scientific interests centred chiefly in plant morphology and he took an especial interest in modes of germination and specialised types of seedling structure. His contributions to systematic botany included publications of the taxonomy of various genera of which the extensive and medicinally important genus strychnos was one. He also edited the supplements to the "Index Kewensis," the *Kew Bulletin*, the *Botanical Magazine* and the "Icones Plantarum." Hill had travelled widely both in connexion with his work and for pleasure and he was a genial and sympathetic companion. He was endued with a strong sense of esprit de corps and cherished a deep affection for Marlborough and King's College, Cambridge, where he was educated, while he regularly attended meetings of such bodies as the Royal Society Dining Club of which he was a member. He will be remembered by many for his kindly acts—he was of those who delighted to do good by stealth.

DARK LANTERN ON RHEUMATISM

THE typical picture of rheumatic fever is sufficiently distinct from that of rheumatoid arthritis for there to be little confusion, but every clinician can remember cases where only the passage of time and the development of the characteristic sequelæ enabled him to make a certain diagnosis. In the age-groups where they overlap the two diseases come to resemble each other more closely; the disease process, too, is of similar type, and thus the nature of the relationship between the two has always excited speculation and conjecture. There are three main theories: first, the characteristically English view that the diseases are ætiologically distinct and that the occasional occurrence of destructive joint changes and heart damage in the same patient is merely coincidental; secondly, as authorities in New York [1] maintain, that the two diseases are ætiologically related and may be manifestations of the same agent in differently reacting types; thirdly, a German view, that there are two types of rheumatoid arthritis, one primary and the other secondary to rheumatic fever. A recen study from the Mayo Clinic might be expected to throw new light on this problem. Autopsies were made on 25 cases of chronic infectious arthritis whose clinical records had been adequately reviewed by a member of the arthritis unit under the able leadership of Dr. Phil Hench.[2] The disease had been present for an average of 7 years, the periods ranging from 3½ months to 30 years. The new light has, however, as so often happens, merely shown up several dark corners. Of these 25 hearts, 14 (56%) showed lesions indistinguishable from those of rheumatic fever; a result on which Hench wisely refuses to comment except in a non-committal way. He believes that these cases represent the presence of two coincidental diseases; but it is a curious distribution since only about 5% of routine post-mortem studies at that centre show evidence of rheumatic fever. As Hench says, additional observations, both clinical and pathological, must be made on many other cases before final appraisal can be attempted. Too often the problems of chronic disease are shelved, like the sufferers themselves, as "lacking clinical interest."

1. Baggenstoss, A. M. and Rosenberg, E. E. 1941, *Arch. intern. Med.* 67, 241.

INSULIN IN THE TREATMENT OF G.P.I.

A. M. San Martin describes what he claims to be a new treatment for general paralysis of the insane by means of insulin in addition to antisyphilitics.[3] A woman was referred to him in whom antisyphilitic treatment and malaria had failed to bring about any improvement. It was decided to try pyretic treatment by means of vaccine, but first, because the patient was in wretched general condition, to give her a high-carbohydrate diet and insulin to improve her nutrition. After she had been treated in this way for a few days it was observed that not only her physical but her mental state also was improved. The treatment was continued and in addition acetarsol was given; in three months' time the patient was able to leave hospital apparently cured. Encouraged by this unexpected success, San Martin has tried a similar method in 9 more cases, combining insulin with bismuth or an arsphenamine preparation. All were patients in whom malarial therapy had failed. In 7 there was striking improvement, 4 being clinically cured; the remaining 2 patients died. In the first case small doses of insulin were given with care to avoid hypoglycæmia; in the remaining 9 hypoglycæmiac doses were given, as for schizophrenia, daily for about 10 days. Antisyphilitics were then begun, and the insulin continued except on the days when the patient received an injection of bismuth or arsphenamine. It is not stated how long treatment went on. Other workers have been using leptazol convulsions or electric-shock therapy in G.P.I.[4] In these convulsive therapy was adopted because mental improvement had not resulted from the usual forms of antisyphilitic treatment. A distinction must therefore be made between treatment aimed at eliminating syphilitic infection (and thus preventing further progress of the disease) and treatment aimed at ameliorating the symptoms which persist after the infection has been eliminated. It has long been recognised that schizophrenic and other psychotic syndromes sometimes occur in the course of G.P.I. Some of these may be merely associated psychoses; others have probably been produced by the syphilitic lesions themselves. The mental improvement obtained in some schizophrenic patients by prefrontal leucotomy suggests that the frontal lobes may play an important part in the symptomatology of schizophrenia. Since the lesions produced by neurosyphilis often affect the frontal lobes, it is possible that schizophrenic changes may be induced by these lesions. Thus, once the syphilitic infection has been arrested, forms of therapy which have been successful in schizophrenia might be expected to succeed in these organically produced schizophrenics. But it must not therefore be assumed that any such new forms of treatment can be a substitute for antisyphilitic remedies.

2. Hench, P. S. 1941, *Proc. Mayo Clin.* **16**, 237.
3. *Rev. méd. Chile*, 1941, **69**, 380.
4. E.g. Kenyon, V. B. and Rapaport, D. *J. ment. nerv. Dis.* August, 1941, p. 147.

Special Articles

THOUGHTS ON A STATE MEDICAL SERVICE

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MEDICAL planning for the postwar era cannot avoid grave mistakes if the broad conditions of life likely to obtain then are not faced at the outset. Two main assumptions are made here which while sweeping in character may not in the time to come be so far fetched as they now appear.

First, it can be safely assumed that the more even distribution of the national wealth which is rapidly taking place will after the war eliminate the richest classes in the community. To have a net income to spend of £10,000 a year under the present taxation means the possession of a gross income approaching the quarter of a million. For a long time to come taxation is not likely to be reduced and to maintain the purchasing value of the saving certificates and war bonds now accumulating will need hard work and hard living for all. There will be too little money available for much to reach voluntary organisations, and the income from charitable sources which has in the past supported the great voluntary hospitals may be reduced to vanishing point. There will also be much less money for the non-panel general practitioners and still less for the consultant. These will no doubt remember the lean years from 1930.

Next, there seems every chance that the income of the wage-earner will depend not only on the trade-union or other rate of pay applicable to his job but also on some system of family allowances. At present only the wage-earner is entitled to the benefits of national health insurance but the net is ever being cast wider and the logical outcome is for the entire family of the wage-earner to be covered by insurance. If the head of the family receives allowances from the state it is no more than common sense that the state should make sure that the family gets the benefit, and how better than by compulsory health insurance?

With these two assumptions in mind the outlook of the medical service serving the postwar community will have to be far different from what it was in pre-war days. Willy nilly we must expect the voluntary hospital as well as other voluntary health organisations to disappear, or at any rate to undergo a revolutionary change from their present position, and must also expect the bulk of the patients who now attend the voluntary hospital or call in the general practitioner to be covered by compulsory health insurance. The future is likely therefore to hold in store a state medical service which will embrace a great majority of the community if not almost the whole of it.

A REAL FAMILY DOCTOR

Bearing in mind—what is sometimes overlooked—that the medical service is for the benefit of the citizen and not for the benefit of the medical profession, is it too optimistic to think of the future insurance practitioner being in charge of say not more than 1000 families instead of not more than 3000 individuals? Instead of the wage-earner going to his "insurance doctor," his wife calling in some other medical man, and his children seeing a welfare-clinic doctor, the school doctor or a doctor at the local voluntary hospital, the entire family as one unit may well be under the care of one medical man. It would admittedly be a big job for that man, but behind him in this imagined state service there would be consultants from the state hospitals with all ancillary services. The state hospital for the district would be surrounded by the satellite special institutions for infectious disease, tuberculosis, maternity and mental cases, and among them would be the "aftercare" and convalescent home, where a period of real convalescence free from all fear of want for the dependent family would put the wage-earner firmly on his feet before he was discharged to face again the struggle of life.

This "family doctor" would be a real one, not one in name only, and he would have to assist him an almoner, a health visitor and a public-assistance officer, working as a team to decide the help needed by all or any members of a family to regain and maintain health. A consulting-room for each family doctor would be provided in the local health centre, where special clinics would be installed such as dentist, oculist, chiropodist, antenatal, tuberculosis and so on. The qualifying curriculum of the medical student would need drastic revision, with far greater training in the maintenance of health and a corresponding reduction in the vast amount of scientific and clinical information which he is now asked to memorise largely for examination purposes. There must of course be compulsory postgraduate training for all, with facilities for research work and training in particular subjects for the future consultants and specialists.

ORGANISATION

The state medical service must be decentralised to the highest possible degree, to ensure that its life is not crushed out by the administration. One can picture a ministry of health of moderate dimensions to implement the policy of the state and exercise a general but not a detailed control over a number of regions. These regions in turn would supervise the individual districts and coördinate the activities of each with others within the region. Some of the special hospitals, for example, might well serve more than one district. Holiday camps and convalescent or aftercare homes also seem to fit into the province of the regional staff. The districts should be as far as possible autonomous within their broad boundaries. Their size must be governed by considerations of geography as well as population, but they would be of an extent compatible with efficiency and economy, each including not more say than 250,000 people or an area greater than a hundred square miles, but depending more on travel-time than distance. The pay and service conditions of the medical staff would be graduated with increments for years of service and higher pay for the more responsible positions, promotion to which would be gained by combined examination and reports of superiors. Pensions, allowances and so on might be based on the conditions of medical service in the Forces. Russia has evolved a national medical service and no doubt we could learn from her experience and profit from her mistakes.

The position of the local authorities in such a national service would require careful consideration, but if districts were of the size suggested the present local authorities would be superseded. The maternity and child-welfare and school medical services would disappear, together with much of the activity of public assistance, district nursing and voluntary organisations such as the C.O.S., I.C.A.A., C.C.H.F., and many others. The out-patient departments of hospitals would be almost entirely emptied, and, with the increasing supervision of the family by the "family doctor" and the support given by convalescent homes and aftercare, many chronic cases would be prevented and the number of hospital beds for all but acute cases might in time be greatly reduced. In fact the success of the family doctors in a district could be readily gauged from the number of hospital beds which had to be maintained. The opportunities for research would be immensely enlarged, and if doctors could be persuaded to keep a careful history of each member of every insured family light would be thrown on the earliest stage of disease of all kinds.

* * *

A state medical service such as here outlined would unify many efforts at present overlapping and conflicting, but could the many interests concerned be persuaded that it would be for the benefit of the community?

COST OF LIVING IN GERMANY.—According to the official index for the cost of living in Germany (*Dtsch. med. Wschr.* Sept. 26, 1941, p. 1074) during July the prices of goods in daily demand were 1·5% higher than in June. This increase is attributed to seasonal influences. The figure for the total cost of living in July was 136·1 (taking the cost in 1913–14 as 100) as against 134·1 for June. The figure for food rose from 130·6 in June to 134·2 in July—an increase of 2·8%. This was ascribed to the more general use of new potatoes which were of course dearer than the old ones. The price of other fresh vegetables also increased. The cost of clothing rose from 158·1 in June to 158·7 in July—an increase of 0·4%.

PORTS OF ENTRY IN POLIOMYELITIS

THE opening of the poliomyelitis season is a reminder that recent experimental work, particularly in the United States, has helped to narrow down the problems relating to the transit of the virus to the central nervous system. Fairbrother and Hurst, in 1929, demonstrated that the virus of poliomyelitis spreads along the axis-cylinders, involving different tracts in the brain serially, and their important work has since been expanded and modified. In their monkeys the nervous system was infected by way of the olfactory tract after intranasal inoculation; from this the idea has taken root in many quarters that infection in man adopts the same path. Bodian and Howe,[1] among others, have confirmed that the axis-cylinders are the lines of communication of the virus, but they have made it clear that ports of entry other than the nasal mucosa should be considered. Some of their evidence has been derived from the study of arrested and non-paralytic examples in experimentally infected animals. Cases of these sorts unquestionably occur in man but their pathological anatomy naturally evades investigation. Bodian and Howe describe changes in 2 chimpanzees and 3 rhesus monkeys which, after administration of the virus, showed spontaneous arrest of the infection with a corresponding limitation of inflammation to foci within the central nervous system. Their first chimpanzee, after being inoculated in the mouth with a virus suspension, developed, a month later, a febrile reaction lasting 24 hours. This was accompanied by a pleocytosis in the lumbar spinal fluid and was followed a day later by a mild and transient left facial paralysis. When the chimpanzee was killed four days after this, the inflammatory reaction was found to be limited to the gasserian ganglia and to foci in the medulla oblongata and cervical cord including the trigeminal centres and left facial nucleus. Thus the disease had apparently been arrested before the characteristic distribution of the inflammatory changes was complete. The second chimpanzee received an intranasal inoculation of the virus and died about a week later of pulmonary tuberculosis, without displaying any clinical signs of poliomyelitis; but microscopic changes characteristic of poliomyelitis were present in the brain, restricted to the olfactory bulbs and secondary olfactory centres.

The site of the lesions within the nervous system in these 2 chimpanzees thus bore a significant relation to the site of the inoculation and this was again shown in the 3 rhesus monkeys which were inoculated intranasally and, after a febrile response, developed no paralyses. Histological examination at periods from one to three weeks later showed restriction of the lesions to the olfactory bulbs, secondary olfactory centres and hypothalamus. In all probability similar localised but arrested inflammations occur in man. Howe and Bodian have investigated the relations between the sites of inoculation and associated changes in the central nervous system in a further group of 6 chimpanzees.[2] In this group, 2 were inoculated by the olfactory, 2 by the oral and 2 by the gastro-intestinal route. One member of each of the last two pairs had the olfactory tracts divided by a preliminary intracranial operation. The resulting attacks of poliomyelitis were milder than those produced by a similar dosage in rhesus monkeys and resembled clinical examples commonly seen in man. All the animals were killed in the acute stage of the disease. Histological examination showed a distribution and intensity of encephalomyelitis which were evidently related to the port of entry of the virus: thus lesions in the olfactory tract were present only in the animals receiving intranasal inoculations while those inoculated in the mouth showed a heavy involvement of the bulbar region, the fifth and possibly the ninth nerves being especially implicated in one animal. In the animals infected by way of the stomach there was histological evidence that the virus had reached the spinal cord first and the brain later. A further point of interest in these experiments was that the virus could be demonstrated in the stools with nearly as much regularity as it can in man. In this the chimpanzee differs from the rhesus monkey which is not susceptible to infection by gastro-intestinal inoculation, and this helps to support the opinion that, where the course of the disease is concerned, zoological affinity carries some weight.

1. Bodian, D. and Howe, H. A. *Bull. Johns Hopk. Hosp.* 1941 **69**, 135.
2. *Ibid*, p. 149.

APPLICATION TO MAN

Howe and Bodian have analysed the lesions in 13 human brains obtained from rapidly fatal cases or cases dying in late stages of the acute illness.[3] They found, like earlier observers, that lesions in the olfactory bulbs and secondary olfactory centres were rare, and that the evidence, taken as a whole, pointed to ingress of the virus by the mouth, pharynx or intestinal tract. The relatively late stage of the disease in these cases unfortunately made it impossible to establish the port of entry more narrowly than this; but in cases showing an initial bulbar paralysis it may be supposed that the oro-pharyngeal mucosa was the site. Sabin[4] mentions, in a recent symposium on poliomyelitis, that during the last ten years a relatively large number of cases of bulbar poliomyelitis have been reported as occurring shortly after tonsillectomy or adenoidectomy performed when poliomyelitis was prevalent. The evidence for the gastro-intestinal tract as a portal lacks precision but it does seem likely, from the anatomical findings in man, that the virus travels from the gut to the spinal cord by way of the sympathetic nerves and by way of the vagus nerve to the medulla oblongata. Sabin and Ward, in mapping out the distribution of poliomyelitis virus in human tissues, have found that it is mainly confined to the nervous system and the alimentary tract, but is not distributed indiscriminately in either; in the nervous system it is found in areas that have undergone pathological alteration, while in the alimentary tract it predominates in the pharynx and ileum. In the absence of any evidence of centrifugal spread of the virus from the central nervous system to peripheral parts, Sabin considers that the intestinal tract is the probable port of entry and that in general the olfactory, respiratory and cutaneous routes can be disregarded. A case of poliomyelitis in a laboratory worker who had been handling the virus, reported elsewhere by Sabin and Ward,[5] is of interest in this connexion. The victim had been washing and grinding tissues from infected cynomolgus monkeys, and the attack—which was accompanied by paralysis first of the right leg and later of other limbs—was fully proved to be poliomyelitis.

Much has still to be learnt of the methods by which virus can travel in the sympathetic system and peripheral nerves. That it does travel in the sympathetic chains appears from the finding by several workers, and confirmed by Howe and Bodian,[6] that transection of the spinal cord will not prevent the progress of virus beyond the level of division. But the virus still spreads in animals sympathectomised at the level of transection, apparently via sympathetic fibres to the gut and thence by the vagus nerve to the brain stem. The same workers estimate[7] the rate of travel of virus along the axon to be 2·4 mm. per hour, a figure which may be compared with the rate of 4–5 cm. in four hours ascribed to methylene-blue by Perdrau in 1937.

3. *Ibid*, p. 183.
4. Sabin, A. B. *J. Amer. med. Ass.* 1941, **117**, 267.
5. Sabin and Ward, R. *Science*, 1941, **94**, 113.
6. *Bull. Johns Hopk. Hosp.* 1941, **69**, 86.
7. *Ibid*, p. 79.

SUPPLEMENT ON ECONOMY IN DRUGS

THE therapeutic requirements committee of the Medical Research Council have added a supplement to War Memo. No. 3 (Economy in the Use of Drugs in War-time), in which additions are made to the classified lists and the categories of certain drugs (indicated by an asterisk in the following list) are changed. The additions are mostly drugs to which approved names have been allotted since the publication of the memo, but some herbal remedies have been added to category C. The substitutes or equivalents suggested are given in parentheses.

(A) *Drugs which are either regarded as essential or readily available.*—Amethocaine, diphenan, coconut oil, hexazole, menaphthone (synthetic vitamin K, 2-methyl-1 : 4-naphthoquinone), mesulphen, orthocaine, soluble phenytoin (sodium diphenylhydantoinate), pholedrine, Pirevan, Piroparv, pyrethrum, safrole, and a large number of sera and vaccines.

(B) *Drugs in the use of which strict economy should be observed.*—Acetylsalicylic acid,* amethocaine, cochineal, diphenan, gonadotrophic hormone from pregnant mare's serum or pregnancy urine, hamamelis,* lobelia,* phenol * chlorocresol, chloroxylenol), phosphoric acid,* progesterone, sodium acid phosphate,* phosphate * and salicylate,* sulphacetamide, sulphadiazine, sulphaguanidine and sulphathiazole.*

(C) *Drugs which are not essential and do not justify importation or manufacture in war-time.*—Celery seed, cummin, euphorbia, galangal, grindelia, hypophosphoric acid and its salts, kola nuts, leptandra, *Mandragora autumnalis*, pennyroyal, raspberry leaves, Rubiazol (sulphanilamide), sarsaparilla, sassafras, serpentary, skullcap, slippery elm bark, liquid and dry liver extract, virginian prune.

Substitutes or equivalents are also suggested for the following unclassified drugs.

Acaprin (Pirevan, Piroparv), Albucid (sulphacetamide), Cignolin (dithranol), Decicain (amethocaine), Mitigal (mesulphen), Orthoform (orthocaine).

The committee remind prescribers that liver extracts are now controlled under a defence regulation which states that they shall be given only to persons suffering from pernicious or other megalocytic anæmia and shall be given by injection only, hog's stomach being used when a remedy for oral administration is required. They again enjoin strict economy in phenol and its derivatives, including the salicylates and aspirin, and say that there is a serious shortage of liquid paraffin which is not likely to be relieved under present conditions. The use of glycerin in medicine is now limited to the manufacture of B.P. and B.P.C. preparations and to the dispensing of doctors' prescriptions. Of the sulphonamides in common use the committee point out that sulphanilamide is the most economical, and urge that sulphadiazine, sulphaguanidine, sulphapyridine and sulphathiazole should be prescribed only when there are special indications.

SOCIAL SECURITY IN NEW ZEALAND

CONTINUING his story (*Lancet*, July 12, p. 51) a correspondent writes: The N.Z. Government had already made one attempt to introduce a universal general practitioner service. In February Hon. A. H. Nordmeyer announced a "panel" system, capitation fee 15*s*. per head (man, woman and child). This was taken up by a few doctors only, chiefly in one-doctor areas, where it has been accepted by all, and works well. As a complete solution for the whole country it failed. A general election being due in November, the tax for Social Security having been collected for 18 months, and the promise of the main benefit (G.P. service) being still unfulfilled, the Minister, at the end of August, proposed a fee-for-service plan. The B.M.A. had not publicly altered its official plan, but it was known that a section, chiefly G.P.s, was willing to consider such a plan. The doctors, however, still considered it a bad time to make any major change, with 25–30% of their number abroad or engaged full time in military duties at home. The N.H.I. committee of the B.M.A. met the Ministers towards the end of August, and subsequently, but as the nature of the new proposals became apparent hostility rapidly developed. The first version was that from a "bottomless pit" a fee of 5*s*. would be paid to the doctor per attendance at his rooms, 6*s*. 6*d*. in the case of a visit to the patient's house, and extras for mileage, &c. It was to be illegal for a doctor to collect fees in any other way. A public outcry was raised, doctors, clergy, chambers of commerce, &c., joining in, and meetings were held all over the country. The Government gave in to the extent of raising the fee from 5*s*. to 7*s*. 6*d*., with extras for night calls, and also in leaving it open for patients to enter into any private arrangements they like with doctors. In this form the proposal became law in September as an amendment to the Social Security Act, the inauguration of the service being postponed from Oct. 1 to Nov. 1. The B.M.A. has announced publicly that practice will go on as usual from Nov. 1. It has also suggested an investigation by a non-political commission. At the time of writing (Oct. 14) the position is thoroughly unsatisfactory. Proposals arising out of party-political interests, bearing no traces of expert medical guidance, and containing no evidence of concern for medical standards or modern requirements, are met by an overworked profession with sullen resistance. Whether the scheme will succeed, in whole or in part, remains to be seen. Whether the profession will be able to come forward with some workable proposals along modern lines also remains to be seen. But Time Marches On. The people are impatient.

SCOTLAND

THE CAMPAIGN AGAINST DIPHTHERIA

THE central health authority has reviewed recent diphtheria experience and is pressing forward with immunisation. Officers of the Department of Health told a recent press conference that 600,000 of Scotland's child population of 1,120,000 had already been immunised and that the aim was to secure as a minimum the immunisation of 85% of the child population—a "target figure" which they believed would largely remove the danger of an epidemic occurring even under the most difficult war conditions. There is little doubt that the immunisation of such a proportion of the child population would secure the desired result, assuming that the under-fives are adequately protected. In the period 1861–65 the mortality-rate from diphtheria in Scotland per 100,000 of the population was 85. Since then the rate has shown a steady and striking fall. In 1931 it was 7, representing in all 356 deaths, with a total number of notifications 8915. From 1931 the number of deaths from diphtheria has shown little tendency to further reduction. Dr. Davidson told the press conference that an average of 400 children died from the disease annually in Scotland in what is called a normal year, that last year the figure was 675, and that in the first half of this year there were 304 deaths. During the last decade the type of infection in Scotland has undergone change. Ten years ago *gravis* infection was rare and it continued to be rare for some years after it had become not uncommon in English Midland towns. Edinburgh, Glasgow, Dundee and Aberdeen have all reported an increasing incidence of *gravis* infection of recent years; whereas five years ago *gravis* infection was relatively uncommon it is now in some Scottish towns the predominant infection. It is not surprising, therefore, that a considerable proportion of fatal cases of diphtheria nowadays are of *gravis* type, although it can hardly be true to say, as appeared in a report of the conference, that "in Dundee over 50 per cent of recent *gravis* cases died." There is need for research into the epidemiology of *gravis* infection, with a view to ascertaining, for instance, whether any particular areas of cities are acting as pockets of *gravis* infection and for the close study of diphtheria among immunised subjects and of fatal cases in particular. One would like to assume that these matters are receiving the earnest care of public health authorities. There can however be no doubt about the wisdom of the central department in urging on immunisation. Criticism would be turned on any delay in adopting such a course. If the people of Scotland have this serious problem set out with honesty of purpose, their coöperation will be secured.

BLOOD TRANSFUSION CENTRES

The Government have agreed to make a grant to the Scottish blood transfusion service towards establishing two centres for the processing of plasma for use in hospitals. One centre is to be under the direction of Prof. J. P. Todd; the other, directed by Dr. C. P. Stewart, is to be equipped with the first plant for the preparation of dried plasma to be used in Scotland. A whole-time mobile blood withdrawal team is to be attached to each centre, so that the services of donors in the country may be used more freely than has been possible.

GRENFELL ASSOCIATION.—This year the association are not printing any Christmas cards. But the work of the mission in Newfoundland and Labrador goes on, and the association is also anxious to help the wives and children of the men who are now serving overseas. So instead of Christmas cards they are asking us to buy picture postcards, which have enough of the snow-and-sledge atmosphere of the north to carry Christmas greetings appropriately, but will also serve as agreeable bearers of everyday messages throughout the year. The cards may be ordered from the hon. secretary of the association, 66, Victoria Street, London, S.W.1, and they cost 2*d*. each.

In England Now

A Running Commentary by Peripatetic Correspondents

THOSE charged with the duty of bestowing names have a responsibility which they do not always take seriously enough. How otherwise are we to account for the extraordinary names that dog defenceless infants through manhood to old age? War tends to add new terrors to these trials of nomenclature when the unprotesting infant is named after a general, a politician, or even a supply dump. Recently our hospital has been involved in a series of exercises involving casualty reception, and it appears that even such exercises must have names. Who chooses the names is not a question for ordinary mortals, but their range is almost as catholic as the pass-words of other days. The psychology of the chooser seems to run in cycles, for after a series of colourless inanimate efforts like axle, truck or station, he will suddenly dart into the very animate—rabbit, hound, ant or bee. It is customary to preface messages about these exercises with the label of the event, and we have from time to time been somewhat staggered to receive an exhortation beginning "Exercise Rabbit," or "Exercise Bee." One's first reaction is to a word of command, and it does seem a little strange, even in these days, to encounter an exhortation to "Exercise Rabbit." "Exercise Bee" is worse, for while the exercise of rabbit can make the exercisor look ridiculous the exercise of bee is not without its dangers. But it is surprising how quickly one drops into the vernacular and comes to receive a whole sheaf of messages all beginning and ending with "Exercise Bee" without the quiver of an eyelid. These messages touch us in two ways. They may send to the hospital a number of "casualties" in flesh or on paper, or they may require us to send some of our surgical pillars out into the wilderness to render assistance elsewhere. We do not complain about these things, though their novelty has worn off. It may be that we are instructed to stand by for the reception of "casualties" from 2 P.M. one day (or from 14·00 hours, as the official word has it) until 8 P.M. next day. Since these performances nearly always embrace Sundays they necessarily cancel week-end leave for everyone, and all that commonly happens by way of compensation is that we solemnly make "nil" returns at two-hourly intervals to a whole host of functionaries, seen and unseen, known and unknown. Usually at some time or other in the course of the performance one batch of "casualties" does arrive on our door-step, sometimes a mere scrap of paper to the effect that it represents *x* patients transferred from another hospital; sometimes a collection of warriors said to be more broken in body than they appear to be in spirit. These visitations usually descend on us in the early hours of the morning, and they inevitably involve the feeding and watering of the convoy attendants, if not of their burdens. Sometimes these burdens announce that they have come to stay for an indefinite period ("until transport can be arranged to take them away"), and, as can well be imagined, this latter development is apt to be coldly received; for the fitter a patient the more nuisance is he likely to be.

When we are instructed to send surgical personnel and equipment into a far country there is much beating of wings. Ultimately two chariots are laden, one bearing the cream of our personnel, the other the miscellaneous collection of equipment that constitutes the stock-in-trade of a mobile surgical unit, and with a triumphant blast they disappear in search of new worlds to conquer. Sometimes these expeditions last only for a few hours, sometimes they extend over night. I have never been privileged to see any of these field operations at close quarters, but I am credibly informed that they can be very entertaining. Sometimes they include a spirited discourse (flippantly referred to as "pep talk") from some military dignitary, the effect of whose oratory may be dimmed by some such untoward and untimely incident as the fainting of a nurse, or the hiccough of a surgeon, both events outwith the pharmacopœia of the performance. Occasionally fate sends our wanderers to spend the night in a country house, where they are treated right royally, to return to us with picturesque tales of well-being that only serve to depress their colleagues, who have been condemned throughou to the everyday. The activities of the peripatet surgeons, like these of the stay-at-homes, never seem assume formidable proportions; they solemnly set u shop and stand like tradesmen awaiting customers in t market square; but customers are scarce. One of th crowning penalties of these exercises is that they ca for the submission of a report on them; and report w do, usually with brevity, occasionally with vigour, bu always in our story adhering to the prescribed ritua beginning as we end, "Exercise Bee . . . Exercise Bee."

* * *

In this country when a public servant fails in foresigh performance or energy we often take away his responsibili ties and elevate him socially. Poor old Jones who mad such a mess of the Ministry of Tics starts a new life o comparative harmlessness as Lord Neuralgia. This admir able method seems to reach almost a Chinese pinnacle o civilisation, but curiously enough the lone, disregarde prophets in the wilderness who suddenly are shown to b right, or at any rate less wrong than the popular prophets are not rewarded and made ministers. There is grudging, insular feeling in the mass of us who have bee mistaken or misled which prevents their immediat acclamation, otherwise we might have recently seen Mr Pritt as Lord Chancellor and Prof. J. B. S. Haldane i some very high post indeed. For years he has been strong supporter of Russia, has preached the essentia soundness of the Soviet system, and is a confirmed Marxist and Leninist. His wonderful little Pelican "Science and Everyday Life," consists of seventy articles he wrote in the *Daily Worker*, and they deal with a glorious variety of subjects in a terse, witty and fearless way—Why bananas have no pips, Do continents move? Atom smashing, Colliery explosions, Genetics. They who have the restraint might read one a day as a tonic. Personally I read the lot at a sitting, and am hungry for more. What admirable broadcasts they would make, but it is more than doubtful whether the B.B.C. would allow them. Yet any one of these little articles would make a most stimulating "go to" talk at 7.55.

* * *

Transfusion centres are apt to grow into monsters and as an itinerant progenitor of these war children one at times feels a little concerned. Is it all being overdone? Have we not already got enough plasma and serum to see us into the twenty-first century, and will not many decades of war have by that time reduced us to such a simple standard of living that our plasma-proteins will have been reduced totalitarian-wise into a standard amino-acid capable of synthesis in the laboratory? With the continuous call for scrap will our hæmoglobin molecule not think it best, in the national interest, to come off the iron standard and use chlorophyll as ersatz? Perhaps before such drastic changes are demanded the liver may be able to achieve a greater economy of iron, salvage of the erythrocytes being effected by the reticulo-endothelial cells to the slogan "use this envelope ten times before discarding it."

* * *

Mention of cucumber seeds with their copper-protein enzyme in THE LANCET of Nov. 8 (p. 571), suggests that I ought to set out my great copper conserving scheme. I suppose it is the result of all these anti-waste slogans, but I find myself developing an anti-waste or salvage mind. I am concerned, in the Quaker sense, with Fehling's solution. All biochemists unite to tell us that Fehling's solution is unreliable and only Benedict's solution should be employed in the clinical laboratory test for sugar. Despite this warning, or perhaps I may now say ukase, the twin bottles for Fehling's test still live side by side in thousands of test-rooms. I cannot boast that I have visited all these thousands, but random sampling, so to speak, has shown that Fehling is never absent. Now my great scheme is to conduct a Fehling's collection campaign. Let us take this chance of a biochemical advance by educating ourselves universally to use Benedict and Benedict only. Let us save copper by collecting all the misused bottles of Fehling's (blue) solution. A simple process will yield copper. If all the Fehling's (blue) solutions now mistakenly displayed in hospitals and consulting-rooms were collected, we should have enough copper to make—whatever is made from copper. I am sure it would save

several shiploads (vide M.O.I. film passim). Details of collection can be worked out locally. The great thing is to sacrifice Fehling in a twin campaign of biochemical efficiency and copper economy. Who was he, anyway?

* * *

The great day had arrived at last, and the A.D.M.S. was due within the next two hours. He was to inspect, of course, the main cook-house of the battalion, and that of a small outlying post, after the good lunch we had arranged to give him had taken its accustomed place in the day's routine. As messing officer I had dealt with assistant directors of medical services before, and knew just what they liked: the spotless roller towel hanging up, the hand wash-basin with the soap laid out conspicuously *and* the nail brush. To the cook-house of the small outlying detachment I sent a young subaltern, with instructions to get the place clean; cleanliness, I explained, was the keynote with any A.D.M.S., and it did not matter so much how the food was cooked, what was being cooked, the qualifications of whoever was cooking it, so long as everything connected with the cooking of it was hygienic. Nor was it vital to see that the contents of the swill-tubs had the correct swills in them, so long as they were clean outside and had the lids on them. I went to my own cook-house for a final look round with a feeling of confidence; everything was completely A.D.M.S.-shape—tables clean, rims of the mustard pot covers shining (a point they are very hot on) and the cooks' faces washed. Those men who seem to be incapable of keeping themselves clean had been liquidated for the morning by the staff sergeant cook. This was going to be a much easier visit to get through than one from one of those expert-on-food generals who may ask awkward questions about the menu, or demand an exhibition in pastry-making from some poor cook. When the victim gets all his quantities wrong from nervousness, the general usually suggests kindly that perhaps he has not done any pastry-making, but has always cooked the vegetables; and the cook will eagerly clutch the straw and agree, whereas he has really been making beautiful apple tarts for the past year. Oh yes, I thought, this would be much easier than that sort of visit.

I went into the back-yard to wait; I should be warned when the party arrived by the main road. That potato must be moved: I bet I can putt it behind the dustbin with my stick in three. One—that was a useful shot. Two—I do wish these A.D.M.S.s would come the normal way and not arrive suddenly by the back entrance. "Good-morning, Sir," I exclaim with a hollow laugh. "Yes, sir, quite a good putt. I was just going to put it in the swill tub." What? Have all my cooks been on a cook's course? This isn't fair, you're supposed to look at my beautifully scrubbed tables. Look at this drain, sir; is it clean? It is! "Well, sir, I am not quite sure if all the cooks have been on courses or not. I shall have to refer to my files. I beg your pardon, sir? How do we make a baked rice pudding?" This is an outrage. What about looking at the cook's spotlessly clean hands, the absence of flies in the larder. Hi! you can't pass that meat-store. We've spent hours cleaning it and chasing the blue-bottles out. Besides there's the new piece of butter muslin over the bacon, specially arranged for you. That's the last straw, passing the mustard pots without picking up one lid to see if it was clean. Not one! And then, to cap all, asking one of the cooks how to make a jam tart. He's only there to look clean. It's not fair, I say; this Army's getting too modern.

* * *

I travelled back from an aunt's funeral the other day with the family solicitor, a judicious, nutty, glass-of-sherry-on-the-sideboard little man. We fell naturally to discussing the old lady and the indomitable pessimism which was her characteristic. Ninety years old in the first week of September, 1939, she philosophically remarked, "Well, I'm afraid this is the last war I shall see." And so it was. The lawyer quoted to me Sam Weller's words to his father—"Well, ve must all come to it, one day or another; there's a Providence in it." And the father's rejoinder—"Of course there is; wot'd become of the undertakers without it, Sammy?" This led us on to his experiences (copious, it seemed) of morticians. He spoke of their tact and their fees. The latter, he thought, were stepped up pretty high, but then the relatives felt it would be disrespectful towards the departed to dispute the bill. "And they always get paid first," he added feelingly, "before the doctors and long before the lawyers." Then he asked if I'd seen that recent prosecution at Liverpool assizes of the two undertakers' men who filled the coffins with sand. In the confusion after an air-raid they had been unable to find the bodies in time; the funerals were overdue, the relatives were waiting and something had to be done. It looked an unsocial and unsettling kind of deception, but, instead of being tried for a public mischief, they were just charged with the offence of making a false entry contrary to the burial laws. They pleaded guilty and their counsel claimed that they were really public benefactors; they had done a charitable act; they thought the corpses must have been interred in a communal grave and they carried on with the funeral ceremony so as not to disappoint the mourners who had assembled to mourn. I asked the man of law how the deception came to be detected. He said the bodies were discovered afterwards. What happened to them? Was there another funeral? He didn't know. Continuing in this macabre vein, he offered me another bit of gossip floating round the undertakers' world. A patient died of some rare disease. His widow acceded to a request from the hospital authorities that they should be allowed to make an autopsy of such an interesting case. The body, with some of the organs removed and rather roughly sewn up, was eventually deposited at the mortuary. Meanwhile a woman in the neighbourhood had given birth to a still-born child, and, not wanting the fuss of a funeral, asked a member of the mortuary staff if he could do anything about it. As another of these "charitable acts," he said he would see what could be done. The sequel was a surprise for a most respectable firm of morticians when its representatives came to prepare the corpse of the hospital patient for decent interment. They found the fœtus inside his empty abdomen. What criminal offence had been committed and what disciplinary action followed I never learnt, for at this moment, rather to my relief, the railway carriage filled up with young men and maidens whose chatter was of livelier things.

* * *

It was the memory that fried tench with mushrooms (or at a pinch sliced young puffballs) is no mean dish that made Uncle take the boy to a pond which he had not fished for thirty-five years. Everything seemed just the same as of old—the smell of the water mint, the reflecting and expectant stillness of the water, even the same old clumps of *Potamogeton natans*. How proud Uncle had been when he learnt that name from an elder brother forty years ago. The white quill float pointed like an uplifted finger, commanding silence; on the other side of the pond the boy's red and green cork one stood perkily, almost aggressively, upright, the moor-hen's lovely yodel came from the rushes at the shallow end, everything seemed exactly the same. "Anything doing?" asked Uncle after a while, lowering his voice for the tranquil carrying water. "I thought I had a nibble just now," said the boy, louder. Probably a lie, a lie in the best tradition, full of hope and optimism. How like that other boy, even the voice. "I've got one, hurrah! By Crumps, it's a wizard. Come and look, Uncle!" "All right, all right, you needn't make all that noise about it. You'll frighten the others." Uncle didn't really mind a hoot about the noise, but he was repressing emotion and was therefore a bit irritable, for that other boy has been dead twenty-four years now, waiting in some Mespotamian sand for the tide of battle to flood again. "Qui procul hinc . . ." Uncle admires the fat pounder, lying in the grass, the fine mosaic of his tiny scales, the gold-green sheen, the ruby eye turned down as though to watch the pouting mouth. Uncle remembers there was a French master who used to make the same sort of lip movements when pronouncing "ou," and they called him The Tench, which degenerated unjustly into Stinker. Uncle relates this trivial incident to the boy who receives it politely as some Chaucerian, or at any rate Edwardian, coarseness. Uncle was about to show him how to distinguish the sex by the pelvic fins; better not. He tiptoes back to his rod resting on the rushes. Thirty-five years! Tench will probably be the same in thirty-five thousand, gobble up brandling, hook, and all, then look surprised when they gasp on the bank. Poor fish. Few come back to teach them, few

come back. But what of us? What was the boy talking about coming along here? Hurricanes and Tomahawks, canon or machine guns. What was that other boy always reading? "Famous Battles," "The Green Curve." We are all poor fishes. The white quill bobs twice and glides under the water.

Letters to the Editor

THE DERELICT SWAB

SIR,—I have read with great interest the annotation on surgery and the common law in THE LANCET of June 7 (p. 729). You very much doubt whether the courts of common law will agree with the surgeon's view expressed by Mr. Zachary Cope, that, if he receives an assurance from the theatre sister that all the swabs and instruments have been accounted for, the surgeon may sew up the abdomen and be relieved of responsibility if one remains inside. I agree with your view that the precautions the surgeon must take to ensure that the swabs are all removed must remain a question of fact in each particular case. The theatre sister's assurance is not a sufficient protection even when supported by that of another member of the theatre team.

May I relate an illuminating experience? Many years ago, in the course of an emergency operation late at night for appendicitis in a child, I inserted a protective swab into the abdomen. The appendix was removed and the incision closed. While driving home in my motor-car the thought suddenly struck me that I had left the swab in the abdomen. I returned to the hospital and questioned the theatre sister, who assured me that the swab had been removed. I then turned to my house-surgeon, who gave me the same assurance. I replied that I was not satisfied, and asked the theatre sister to count the swabs before me. She did so, and one was missing. I had the patient returned to the operating theatre, and removed the swab.

This experience led me to adopt the view that it is the surgeon's duty to accept the responsibility for a derelict swab. If he makes an invariable practice of never putting a "loose" swab into the abdomen, he will never leave one there.

Adelaide. H. S. NEWLAND.

ENURESIS

SIR,—Dr. Raymond Greene wonders why I should think it relevant to mention cases of exanthemata occurring after the onset of enuresis. The answer is that enuresis often takes a turn for the worse after one of these infections; this was so in a large proportion of my cases. The difference between cases showing much dilatation of the upper urinary tract and cases showing little was that the greater the dilatation the more constant the evidence of infection in the urine. So well does this rule apply that in the lesser degrees of dilatation, so commonly seen among enuresis cases, it is unusual to find evidence of infection in the urine at all; but where infection does exist it is relatively easy to get rid of it. In cases where there is much dilatation, however, it may be impossible to achieve sterile urine; modern urinary antiseptics often reduced the degree of infection, but failed to clear it up completely. The difficulty in attaining this end usually seemed to have a direct relationship to the amount of dilatation present. The involvement of the urethra in the inflammatory process in all the cases of vulvitis was a personal observation. Usually it could be detected by merely inspecting the external urinary meatus. I duly acknowledge the correction concerning the sites at which the ducts of the glands of Bartholin open.

My studies on the calibre of children's urethras were always made under general anæsthesia at the termination of an endoscopy, on patients whose urinary tracts required such investigation. It would be difficult to find an objection to such a procedure on psychological grounds. The question whether there might be any relationship between benefit from treatment and a threat of a further instrumentation can be answered finally now and in the negative. Since the treatments were carried out under a general anæsthetic the patients had no knowledge of what was done or of what might be done on a future occasion.

I can assure Dr. Arnold Heymann that in my experience spina bifida occulta, epilepsy or idiocy have no relationship to the great majority of cases of enuresis. I went carefully into the question of spina bifida occulta in a number of patients. Every case of enuresis with threadworms was admitted to hospital and given treatment to get rid of the parasites. I was never able to satisfy myself that they were a causal factor. Since enuresis is more common among the under-nourished than the well-nourished it would be surprising if an improvement in the diet of the former did not reduce the incidence of the complaint. The signs of inflammation at the neck of the bladder in cases of enuresis are not likely to be seen by the cystoscopist unless the child is in the lithotomy position, because they are usually present only at and adjacent to the internal urinary meatus. It would be unreasonable to assume that they are caused by the instrument when an inspection of the posterior urethra shows more important inflammatory changes in the immediate vicinity. The question of how many leucocytes in the urine are to be regarded as evidence of infection is one I am not prepared to debate.

Harley Street, W.1. H. P. WINSBURY-WHITE.

SIR,—Dr. MacLeod's voluntary and diurnal attack from the heights has damped but not drowned me. I am sorry that he found "turbid" a letter which some have found lucid to the verge of the brutal, and surprised that he should have bothered about a criticism which he a little rudely dubs "senseless" and unworthy of a serious reply. My question about the relation between dilatation and infection, which seems to have caused him so much annoyance, may be clearer to him if I put it this way: if patients have both upper urinary tract dilatation and infection below, how does one know which is primary with enough certainty to divide the cases into two groups? As to Bartholin's glands, Dr. MacLeod will, I hope, forgive me if I refuse to embark on a lecture on elementary anatomy. It will save us both a lot of time if he will refer to Gray's "Anatomy."

Whitchurch, Aylesbury. RAYMOND GREENE.

CARLOS FINLAY AND YELLOW FEVER

SIR,—I am fully satisfied with the general trend of your criticism of my book on my father's work on yellow fever (Aug. 9, p. 167), but must clear up some misunderstandings in connexion with his experimental cases. Owing to their lack of severity and their small number in comparison with the inoculated cases you are right in sustaining that they cannot, by themselves, be considered as proof of his theory—this required the later sanction of the more convincing experiments of the U.S. Army Yellow Fever Commission—but what I consider unjust is the supplementary statement, made in most Anglo-American writings, that he did not produce any positive experimental cases. This statement is based solely on the ground that his positive results did not comply with the narrow time-limits fixed by the commission, limits which later investigations have proved not to be as exact as at first supposed. As regards the incubation period in man my father's views have always coincided with those of the commission in that yellow fever is only infective in the first days of the disease, protracting the infective period up to the sixth day. N. P. Hudson and C. B. Philip, however, proved in 1929 (*J. exp. Med.* **50**, 583) that yellow-fever monkeys are "mosquito-infective" before the appearance of fever, all through the febrile period and even after death. As regards the duration of the extrinsic incubation period, J. H. Bauer and Hudson in 1928 (*Ibid*, **48**, 147) showed that the yellow-fever virus can be transmitted through the bite of the mosquito on or after the 9th day. Aragão noted in 1929 (*Brazil-med.* **43**, 1481) that one lot of mosquitoes became infective as early as 4 days after ingestion of the virus, and in 1932 N. C. Davis (*Amer. J. Hyg.* **46**, 163) showed that:

"1. The extrinsic incubation period of yellow fever in *Aëdes ægypti* was shortened at high temperatures and prolonged at low temperatures.

2. The ability to infect was acquired after 4 days at an average temperature of 37° C., after 5 days at 36° C., and 6 days at 31° C.

3. When stored at room temperatures averaging 25·1° C. *Culex stegomyia* mosquitoes became infective at the end of 8 days; when the room temperature was 23·4° C. they were infective when tested at the end of 11 days but not at the end of 9 days.

4. Infectivity appeared after 18 days at 21° C.
5. Mosquitoes were not infective after 30 days at 18° C."

This shows that the basis of a too short mosquito incubation is wholly insufficient to lead us to discard my father's positive cases in the presence of other data such as proper preliminary isolation; clinical symptoms of mild yellow fever (sudden onset, followed by a febrile course with a remission on the second or third day and a final defervescence, accompanied by slowing of the pulse, bleeding of the gums, albuminuria and jaundice); followed by immunity through a span of years of living in a country where yellow fever was endemic. It would have been more satisfactory if my father had allowed his infected mosquitoes to incubate longer, but although he realised this possibility as far back as 1891 (p. 78 of my book) conscientious scruples held him back, limiting his objective to the immunising of his inoculated subjects by mild attacks of yellow fever, even if this meant that his findings were not always convincing to others.

Havana. C. E. FINLAY.

GRADUATION AT AN EARLIER AGE

SIR,—Dr. Paterson's article leaves me a trifle perplexed. Surely the bright boy can still matriculate at 16, take his first M.B. examination from school or from technical college and enter his medical school at 17. Is it true that he is now *compelled* to wait until 18 or 19 before starting his medical training at all? There are some for whom it is financially necessary to complete their training as soon as possible. Such was my own position and I would therefore think it a pity to force those in like case to turn to other fields. But I would not argue from this that qualification at or about 21 is a good thing. For one thing it involves some sacrifice in general education, and for another it forces the individual to assume even during his student years responsibilities for which he may not be sufficiently matured.

Dr. Paterson states that it is a "psychological fact" that the intellect of a boy of 16 has already been mature for two years. I am sorry but I do not believe him unless he is using the word in a sense all his own. The term is a hard one to define; intelligence, it has been said, is what a psychologist measures when he measures intelligence, but even adopting this pragmatic definition there is evidence to suggest progressive maturation until at least 16. If other aspects of mental life be brought into consideration (and they cannot be left out) the process of maturation continues far longer. Indeed, there are matters which one can "learn" at 30 which would be beyond one's scope at 20.

In general, therefore, it would surely be better to encourage, though not to compel, the medical student to carry his general education a little further and to qualify a little later. Apart from Latin and Greek, I should think that he would benefit from some knowledge of philosophy and statistics which he now sadly lacks! I agree that this raises the whole question of late marriage, which would surely be better solved by state scholarships on an adequate scale. If we are to have in the medical profession those who are really suited to it and not just those whose finances will stay the course, some such subsidy will be necessary anyway.

The Cassel Hospital. C. H. ROGERSON.

ACUTE POLYRADICULONEURITIS

SIR,—The advancement of medicine must necessarily be associated with the appearance of new terminology, yet today there seems to be a facile tendency for the adoption of nomenclature and phraseology, particularly if highly sounding or of continental origin, without sufficient regard for their soundness or suitability. In some instances, this may be due to the inherent inferiority substratum in the British character which permits the belief that native enterprise is of a lesser quality than that of the foreigner. One sees this feeling prevalent in most intellectual spheres, whether music, art, science or medicine, and one wonders why. It was probably this self-effacement rather than the desire for progress which led to the eager adoption in this country of the Basle anatomical nomenclature, a scheme sponsored mainly by a collection of German booksellers to whom such expressions as Astley Cooper's ligament or Hunter's canal were anathema.

The term radiculoneuritis came into prominence about 1916 and may have originated in France. Recently, it has been used to refer to a condition generally known as acute polyneuritis. Those who employ the new edition do so no doubt because they consider it to be an improvement, thereby indicating indirectly that involvement of the nerve roots is of sufficient importance to warrant its inclusion in the title of the disease; whereas in fact it is known that the most evident lesion is found in the extraspinal portion of the nerve tract. Thus, Holmes in his series of cases declared that examination of the nerve roots disclosed no abnormality whatsoever and this finding seems to be general. It should also be remembered that anatomically the term radicular nerve is often applied to the conjoined portion of the nerve roots formed by the junction of the anterior and posterior roots. An inflammatory lesion affecting this portion of the nerve tract could quite properly be called radiculoneuritis. Thus the term itself can hardly be considered an improvement on anatomical or pathological grounds, nor does the clinical side furnish any additional support. The picture of an acute spreading paralysis may be produced by some half-dozen conditions all of which show certain changes in the spinal cord. This finding applies also to acute polyneuritis in which the toxic process shows a selective affinity for the neurone as a whole, so that the term polyneuronitis as suggested by Russell Brain is in this respect more suitable. But in the absence of a more exact knowledge concerning the nature of the malady there seems little point in substituting one inadequate designation for another, even though it may sound more modern.

London, S.W.3. J. H. MULVANY.

LIGATION OF PATENT DUCTUS ARTERIOSUS

SIR,—To those cardiologists whose enthusiasm has been fired by the brilliant exploits of some of our thoracic surgeons, I commend the perusal of a thoughtful and temperate address on the Newer Surgery of the Heart and Large Vessels, by H. M. Marvin (*Bull. N.Y. Acad. Med.* October, 1941). The operation mortality of ductus ligation in these American cases is astonishingly low—only 4 operation deaths out of 42 cases. Nevertheless, like Mr. Mulvany, I wonder if this operation is often justified. Surely the predisposing factor towards bacterial endocarditis in these, as in other cases, is the presence of an avascular bed, on which bacteria and fibrin are deposited from the blood-stream. Ligation of the ductus can only modify the conformation of this avascular bed, and in any case by the time the diagnosis is made bacteria and clot have probably already been implanted in the pulmonary artery opposite the entrance of the ductus. I agree again with Mr. Mulvany in the possibility of an arrest, and perhaps of cure, of bacterial endocarditis in these patients without surgical treatment. I have at present under my observation a lady who has been symptomless and working since September, 1940, after treatment in February, 1940, with heparin and a sulphonamide of a bacterial endocarditis implanted on a patent ductus.

With regard to the non-infected case, it will be interesting to see what is the expectation of life where ligation has been performed during infancy or childhood. But we may have to wait for many years before evidence is convincing that life is prolonged by this somewhat hazardous operation.

London, W.1. MAURICE CASSIDY.

VITAMIN E

SIR,—In your leading article of Aug. 23 you reviewed the literature on vitamin E in the treatment of muscular dystrophy and motor-neurone degenerations. Your conclusions were that vitamin E is of little practical value, though "that there is something behind this no-one can doubt." The leading article in the *British Medical Journal* this week states: "We find nothing yet to persuade us that any human disease or any disturbance of childbearing or locomotion in man is due to a deficiency of vitamin E, or is alleviated by treatment with it." I have read again the papers on which these two leading articles were chiefly based, and I cannot agree that they justify any statement that vitamin E is of little or no value. To avoid repetition I shall only examine in detail those papers dealing with muscular dystrophy, since the same criticisms are applicable in part to the papers on nervous degenerations and, indeed, to the treatment of all deficiency diseases.

In muscular dystrophy some muscle-fibres are normal, some are completely replaced by fibrous tissue, and some are degenerating but are still present. It is only the function of these latter fibres which can be improved by any form of treatment. In children getting worse rapidly there are many such fibres, and so a great improvement is possible. In adults, in whom the disease has been slowly progressive for many years, there are only a few degenerating fibres present at any one time. The muscular weakness is essentially due not to these fibres but to the loss of those which have completely degenerated during the long course of the illness. In adults, therefore, little or no improvement is ever possible, though the disease can be arrested. Bearing these facts in mind the negative results of vitamin-E therapy reported from the Mayo Clinic (Eaton, L. M., Woltman, H. W. and Butt, H. R. *Proc. Mayo Clin.* 1941, **16**, 523), by M. M. Doyle and H. H. Merritt (*Arch. Neurol. Psychiat.* 1941, **45**, 672), and by G. Fitzgerald and B. McArdle (*Brain*, 1941, **64**, 19) lose much of their significance, since in a total of 20 cases treated only 5 were children. J. W. Ferrebee, W. O. Klingman, A. M. Frantz (*J. Amer. med. Ass.* 1941, **116**, 1895), however, have also reported negative results in a series of 13 children, so that there are 18 cases in all which have not responded to treatment. These, numerically, are more than balanced by the children who have improved, according to S. Stone (*J. Amer. med. Ass.* 1940, **114**, 2187; *J. Pediat.* 1941, **18**, 310), G. E. Donovan (*Lancet*, 1940, **2**, 162) myself, and various personal communications from England and abroad. There are several explanations of these contradictory reports.

. . . *importance of not giving too much vitamin E.*—All the children who have improved have been given vitamin E either as whole wheat germ or as wheat-germ oil and yeast, the amounts not greatly exceeding those which could be taken in food. The children who have not improved have all had synthetic vitamin E as well as, or instead of, the natural forms, and the total amount taken has been very large. Most of the children, indeed, received so much vitamin E that they could only have obtained the same amount from their diet had they eaten each day three times their own weight of bread from which the wheat germ had not been removed. It seems most unlikely that these amounts of vitamin E can ever be required, while it does seem likely that they are harmful. For the muscles themselves probably destroy any surplus of vitamin E, and therefore their degeneration is likely to be hastened when they are confronted with the strain of destroying amounts of vitamin E many times as large as could ever be provided by any diet.

. . . *importance of giving other vitamins and zinc and manganese in their correct proportions.*—There should be some relationship between the amounts of the various vitamins, and also minerals, in the diet. For instance the storage of vitamin A is affected by vitamin E, vitamin D needs a certain calcium-phosphorus ratio to develop fully its antirachitic activity, and there is an optimum ratio between manganese and vitamin B for preventing the toxic effects which occur when large amounts of either are taken. It seems that those minerals and vitamins which are especially necessary to each other for their mutual metabolism by the animal body generally occur together in vegetable foods. So though we do not know enough to give the correct balance of vitamins and minerals by synthetic preparations, we can solve the problem when treating deficiency diseases by giving foods very rich in the particular vitamin the deficiency of which is causing the symptoms. In this way we shall automatically keep the correct proportions of the related vitamins and minerals and avoid the risk of excessive doses. In the case of vitamin E whole wheat germ is the best preparation, containing not only the B complex but also zinc and manganese, the distribution of the last two in foods being the same as that of vitamin E. Looked at from another point of view, once one postulates a deficiency of vitamin E one must also postulate a deficiency of all those substances chiefly found with vitamin E, and so one must give them as well.

. . . *importance of treating sepsis.*—Any mild chronic or recurrent sepsis, such as carious teeth or frequent colds, completely prevents any response to vitamin-E therapy. Probably the absence of any sepsis would have been emphasised in the negative reports on the value of vitamin E had its importance been realised. As sepsis is not mentioned in these reports it seems possible some children failed to respond because of some mild infective focus.

The disordered creatine metabolism of muscular dystrophy has been investigated by Fitzgerald and McArdle in 2 children for periods of 26 and 36 days respectively, and by Ferrebee, Klingman and Frantz in 2 children for 10 days. Vitamin E given throughout the investigations did not improve the metabolism of creatine. This was to be expected, partly because clinical improvement seldom occurs in under eight weeks and partly because the children were receiving excessive amounts of synthetic vitamin E.

Wimpole Street, W.1. FRANKLIN BICKNELL.

DAY NURSERIES

SIR,—Your report in last week's issue of the conference on day nurseries shows that a point was raised there which has usually been ignored in the past, and which in my opinion is not being stressed sufficiently even now. Most child psychiatrists would agree with me that the child's greatest need during its earliest years is for a mother's affection and attention. This is essentially a strongly *personal* relationship and cannot be adequately replaced by any nursery school however well run. Marguerite Dobbing's experience, as given in her letter to the *New Statesman*, is another discovery (however belated) of a truth that has been preached by child-guidance workers for some years. Miss Anna Freud hit the mark when she said, "Nursery schools had never been meant as a substitute for the home any more than welfare clinics did away with the need for the mother's care or child-guidance clinics with the need for education by the parents." The nursery school is not a home, and even a bad home is better than no home at all. The intuitive understanding on the part of mothers of this relationship with their children has a great deal more to do with the slow progress of the nursery-school movement than is generally appreciated. Just as many a mother, quite rightly in my opinion, clung to her child when the evacuation scheme was launched, so today she will only use the nursery school as a last, often desperate, resort. The care of an aunt or granny, as your report implies, is preferred as being more satisfactory. (With regard to evacuation, many a mother has told me: "I just couldn't send him away, he would never get over it.")

We must recognise that the break-up of family life occasioned by the war is a serious evil and not the least serious outcome of war conditions. I agree with Anna Freud that the nursery schools are trying to fill a serious gap, but we must admit it is only a second best. (There is a real danger that they may be used to blanket those essential social and economic reforms which are so seriously needed to maintain an adequate family life.) With her, I would plead for some place to be found in the scheme for the mother herself. For only in the security of the intimately personal relationship between mother and child can the child develop a real and stable character.

If further confirmation of these views were needed it is to be found in the experiences of the Jewish communal colonies in Palestine. There both mother and father work (on the land) and the children are cared for communally by skilled nurses. None the less, it has been found necessary, in order to get the best results, to allot definite times each day when the parents can take charge of their children. I recommend a study of the development of these communal nurseries to all interested in child welfare.

Leeds. H. EDELSTON.

TOWARDS A NATIONAL SERVICE IN CLINICAL PATHOLOGY

SIR,—Dr. Ponder's statement that the "comprehensive pathological service" now functioning in the county of Kent is "very much on the lines indicated" is hardly correct. The view expressed and reiterated by myself was that by its very nature clinical pathology can only properly be practised "in laboratories forming an integral part of a large and active hospital"; that it can only function properly "in a laboratory which is part of an institution for the treatment of the sick"; and further that it can only properly be practised by those in close and continuing touch with clinical work. On his showing the service described by Dr. Ponder meets neither of these fundamental requirements.

Wolverhampton. S. C. DYKE.

Public Health

Health of New Zealand

THE annual report for 1940–41 of Dr. M. H. Watt, director general of health, records an exceptionally healthy year in an exceptionally healthy part of the world where public medicine has reached a high level of efficiency and is extending towards a complete national medical service. The European population of New Zealand in mid 1940 was 1,546,312, its birth-rate was 21·2, the highest rate since 1925, and its death-rate 9·25 against 9·2 in 1939. Infantile mortality, for which New Zealand has long held the blue riband of the world, sank to the record low level of 30·2. Of the 990 infants who died in the year, 521 failed to survive a week and 630 failed to survive a month. The neonatal mortality has remained almost unaltered at about 22·5 per 1000 live births for many years. Rather more than half of the deaths within the first month are certified as due to prematurity alone, but since prematurity is not per se a cause of death this means that about half of the neonatal mortality is unexplained and in the present state of our knowledge is inexplicable. Tuberculosis mortality was 388 per million, which is a low record for New Zealand, and, we believe, for any community exceeding a million. Cancer mortality, at 1202 per million, would on standardisation for age and sex work out to be not much different from our rate of 1600.

The statistics of the Maori population tell a different story. Their birth-rate was 48·9, infantile mortality 87·2, crude death-rate 17·5 and tuberculosis mortality 4132 per million. Excluding tuberculosis, the death-rate among Europeans would be 8·86 and amongst Maoris 13·37, so tuberculosis alone accounts for not quite half of the higher death-rate among the Maoris. Until recently, the native population of New Zealand, unlike those of the African dominion, colonies and protectorates, was little infected with syphilis, but this has changed for the worse in some districts. The health department is fully alive to this and is taking active steps to combat the spread of syphilis among the Maoris.

Among the many interesting sections in the report is that dealing with hydatid disease, which is probably more common in the islands—especially in the South—than in any other part of the world. There are about 120 new cases with 16 deaths each year, and the incidence does not decrease. When we hear that about half the sheep and cattle in New Zealand have livers or lungs infected with hydatid cysts and more than a third of the country dogs harbour the adult *Tænia echinococcus*, we do not wonder at the frequency of the human disease, or why it does not diminish. Measles, which three years ago spread over New Zealand in epidemic form of exceptional severity for modern times, caused but one death in 1940.

Infectious Disease in England and Wales

WEEK ENDED NOV. 1

Notifications.—The following cases of infectious disease were notified during the week: smallpox, 0; scarlet fever, 1204; whooping-cough, 1955; diphtheria, 915; paratyphoid, 35; typhoid, 20; measles (excluding rubella), 624; pneumonia (primary or influenzal), 553; puerperal pyrexia, 118; cerebrospinal fever, 102; poliomyelitis, 23; polio-encephalitis, 1; encephalitis lethargica, 2; dysentery, 123; ophthalmia neonatorum, 79. No case of cholera, plague or typhus fever was notified during the week.

The number of civilian and service sick in the Infectious Hospitals of the London County Council on Oct. 29 was 1296, including scarlet fever, 165; diphtheria, 297; measles, 22; whooping-cough, 492; enteritis, 21; chicken-pox, 31; erysipelas, 25; mumps, 5; poliomyelitis, 6; dysentery, 27; cerebrospinal fever, 10; puerperal sepsis, 12; enteric fevers, 36; german measles, 1; other diseases (non-infectious), 81; not yet diagnosed, 65.

Deaths.—In 126 great towns there were no deaths from scarlet fever, 2 (0) from enteric fevers, 2 (0) from measles, 9 (3) from whooping-cough, 22 (1) from diphtheria, 59 (3) from diarrhœa and enteritis under 2 years, and 11 (1) from influenza. The figures in parentheses are those for London itself.

There were 7 deaths from diarrhœa at Manchester, 5 at Liverpool and 5 at Birmingham.

The number of stillbirths notified during the week was 157 (corresponding to a rate of 32 per thousand total births), including 17 in London.

MEDICINE AND THE LAW

The Diabetic Motorist

THE Belfast magistrate has dismissed an application by the police that a diabetic doctor should be deprived of his driving licence. The police contended that the reactions to medical treatment rendered the patient unfit to have proper control of a car. The physician to the biochemical department of the Royal Victoria Hospital, giving evidence for the motorist, expressed the view that, provided diabetes was properly controlled by insulin, there was no reason why the patient should suffer incapacity from insulin coma; he himself had some 3000 patients under treatment, including, along with many private motorists, bus drivers and engine drivers, and had no reason to suppose them a danger to traffic. The magistrate, observing that this was the first case of the kind in his experience, was not prepared to give effect to the application of the police and, in effect, disqualify possibly thousands of drivers who use the roads today with as much safety as persons who do do not suffer from diabetes.

The law in Northern Ireland is much the same as in Great Britain. According to section 5 of our Road Traffic Act of 1930 an applicant for a driving licence must "make a declaration in the prescribed form as to whether or not he is suffering from any such disease or physical disability as may be specified in the form . . . or any other disease or physical disability which would be likely to cause the driving by him of a vehicle . . . to be a source of danger to the public." If from the declaration it appears that the applicant does suffer from any such disease or disability, the licensing authority must refuse the licence. The form, as last prescribed in 1937, asks the applicant specifically to declare epilepsy or sudden attacks of disabling giddiness or fainting, any defect in movement, control or muscular power of either arm or leg, or any other disease which would be likely to cause his driving to be a source of danger to the public. While the police are quite entitled to prove, if they can, that a particular diabetic is unfit to drive, it would not seem proper to allow them to insert (in effect) the word "diabetes" in the prescribed form along with the word "epilepsy" if the Minister of Transport (or his equivalent in Northern Ireland) has not done so.

Obituary

FRANCIS CHARLES MARTLEY

M.D. CAMB., F.R.C.P.I., D.P.H.

Dr. Martley, who died on Nov. 2 at the age of 76, will be best remembered for the part he played in the welfare of the Medical Sickness, Annuity and Life Assurance Society. He was vice-chairman of the society in 1908 before it became a mutual assurance company and in 1930 was elected chairman of the board of directors, holding this office until his death. He had a quite unusual ability for figures and correlation of facts and though the small amount of Irish in his make up was occasionally evidenced by a provocative remark, it meant nothing for behind it one could see a kindly pair of eyes and a hidden smile. No-one could have laboured longer or more faithfully than he did for the society, the success of which was a source of great satisfaction to him, and his wise counsel will be greatly missed.

Francis Charles Martley was born in Dublin, and was educated at Rugby and Cambridge, where he took the natural sciences tripos in 1887. He entered St. Mary's Hospital with a science exhibition, qualifying in 1890, and later taking many higher diplomas. After being house-physician at St. Mary's and practising for a while at Buckhurst Hill, he went back to Dublin as demonstrator of chemistry at the R.C.S.I., and anæsthetist to St. Stephen's Hospital. In 1908, however, he returned to London as assistant in the inoculation department at St. Mary's, where he remained on the active staff for thirty years. At first he was largely engaged in teaching workers from all parts of the world, who came to learn

about the opsonic index. In later years he was chiefly interested in blood grouping and carried out some research bearing on its value in paternity cases, in the course of which he made the interesting observation that group two (Moss) corpuscles phagocytose some 25% more bacteria than do group four corpuscles.

Dr. Martley married in 1892 Adelaide Amelia Strangman, who predeceased him in 1935. He leaves a son and two daughters.

STUART ALEXANDER TIDEY

M.D. LOND., M.R.C.P., S.F.D.

Dr. Stuart Tidey, who died on Oct. 29, at the age of 84, was born in Reading. His father was an artist and his childhood was spent largely at schools in Corsica, Switzerland and Germany. He studied engineering at the Crystal Palace for two years before he entered St. Mary's Hospital, where he graduated in 1886, later taking the M.D. Lond., the M.R.C.P. and the Swiss federal diploma after further study at Geneva. He had held the posts of H.S. and assistant pathologist at St. Mary's, and in 1890 he started practice in Montreux, remaining there until 1912 except for a brief interval in Florence, where he followed StClair Thomson. At Montreux he had a large practice both on the lakeside and at the climatic stations on the hills above. But his health giving cause for anxiety he went to settle in British Columbia where, after farming for a bit, he took the state diploma in medicine and joined John Antle's medical mission to loggers. The last war found him, though already 56, ready for fresh work, and he helped to fit out the hospital ship *St. George* and worked there till 1917 when he joined the medical staff of the Middlesex War Hospital, near St. Albans. Still spoiling for adventure he served 1920–31 as ship's surgeon for the Elders & Fyffes line. Very quiet and rather rugged in manner, L. P. writes, he always knew his job and the latest developments in it. He would come almost unobserved into a medical board at Napsbury and almost immediately he would say the few words making points that were in danger of being missed. His writings were few for a man of his originality and vigour; apart from some handy guide and travel books he published his experience of the use of compression in pulmonary lesions and of the drainage of empyema. He loved to discuss these matters and specially enjoyed any argument against his own theories.

At the age of 73 Tidey retired to Edgware where he could indulge his tastes for music, natural history and gardening. The progress of parkinsonism curtailed his physical activities, but he retained his mental alertness to the last. He married Georgiana Booth, who predeceased him, and leaves two daughters.

Medical News

University of Cambridge

During October the title of the degrees of M.B., B.Chir. was conferred on E. H. M. Gillieson and R. M. Stevenson.

Royal College of Physicians of Edinburgh

At a meeting of the college held on Nov. 4, with Prof. Charles McNeil, the president, in the chair, Dr. Benjamin Reid (Hellingley, Sussex), Dr. J. L. Cowan (Penicuik, Midlothian), Dr. A. J. Rhodes (Edinburgh), Dr. A. D. Stewart (Edinburgh), Dr. Alexander Joe (Edinburgh) and Dr. J. B. Borthwick (Edinburgh) were elected to the fellowship.

Advisory Tuberculosis Committee

The name of Dr. Ernest Ward should have been included in the Ministry of Health committee on tuberculosis published in THE LANCET (Oct. 11, 1941, p. 437).

Prisoner of War

W.S./Captain J. H. Annan, M.B. Edin., R.A.M.C., has been posted as a prisoner of war.

Royal Society of Medicine

Short papers will be read at the meeting of the section of pathology on Tuesday, Nov. 18, at 2.30 P.M. On Nov. 20, at 2 P.M., the section of dermatology will hold a clinical meeting. On Nov. 22, the section of orthopædics will meet at Orpington Emergency Hospital, Kent, at 11.15 A.M., when Mr. C. Lambrinudi will deliver his presidential address. He will speak on the rôle of orthopædics in medical education. Short papers will also be read by other members, and in the afternoon there will be a demonstration of cases.

King's Physician

Lieut.-Colonel (temp. Colonel) Sidney Smith, F.R.C.P., R.A.M.C., has been appointed hon. physician to the King in place of Major-General R. C. Priest who has retired.

From Strasbourg to Strassburg

After an interval of twenty-three years the German University of Strassburg has opened for the winter session (*Dtsch. med. Wschr.* Sept. 19, 1941, p. 1046). Applications for admission were received from all parts of the Reich but those from Alsace were given preference and Alsatians form the bulk of the students. The new university has four faculties—law, medicine, philosophy, and science, and of the 100 lecturers who have been appointed, 30 hold posts in the faculty of medicine.

Presentations to Dr. Barnes

On Oct. 30 Dr. Stanley Barnes, retiring dean of the faculty of medicine of the University of Birmingham, was presented by the United Hospital with his portrait, painted by Mr. Harold Knight, R.A., in recognition of his many services over many years in the reconstruction and administration of the new medical school and hospitals centre. The Lord Mayor, who made the presentation, said that Dr. Barnes had been a master builder, and Prof. W. H. Wynn, M.D., who also spoke, acclaimed him as a brilliant physician, man of affairs and great citizen. In reply Dr. Barnes said that he had felt constrained to alter the career he had laid out for himself in research in medicine in order to take his share in the development of medicine in the midlands. His loss of private practice did not matter but he had also had to sacrifice some of his hospital work which, he said, "to me was the first element in my life." Dr. Barnes received a George III silver pint pot from the council of the university, the senate and the members of the faculty of medicine, and the medical students have also given him a piece of silver plate.

Appointments

BROADBENT, BERNARD, M.B. Camb., D.P.H. : deputy M.O.H. for Tottenham.

DAVID, GEORGE, M.D. Berlin, L.R.C.P.E.: temp. asst. M.O. for Hounslow.

KEMP, T. A., M.B. Camb., M.R.C.P. : medical registrar and blood transfusion officer at St. Mary's Hospital, Paddington.

Births, Marriages and Deaths

BIRTHS

FORRESTER.—On Nov. 8, at Llanelly, the wife of Dr. G. Stuart Forrester—a son.

FRENCH.—On Nov. 4, at Rawalpindi, the wife of Capt. J. M. French, I.M.S. (of Burgh Heath, Surrey)—a daughter.

HODGKINSON.—On Nov. 6, at Milford-on-Sea, Hants, the wife of Dr. H. L. Hodgkinson—a daughter.

JOY.—On Nov. 8, at Frome, the wife of Captain David Joy, R.A.M.C.—a son.

LASCELLES.—On Nov. 4, at Farnham, Surrey, the wife of Surgeon Commander W. F. Lascelles, R.N.V.R., Yarm, N. Yorks—a daughter.

MACDONALD.—On Nov. 7, at Barnt Green, near Birmingham, the wife of Captain William Macdonald, R.A.M.C.—a daughter.

ROBERTSON.—On Nov. 3, at Perth, the wife of Captain R. P. Robertson, R.A.M.C.—a son.

RYDER RICHARDSON.—On Nov. 6, at Whitchurch, Aylesbury, the wife of Dr. J. C. Ryder Richardson—a son.

WELLS.—On Nov. 6, at Oxford, the wife of Dr. L. R. A. Wells, St. Olave's Hospital, London—a daughter.

YOUNG.—On Nov. 10, at Woking, the wife of Dr. B. A. Young—a son.

MARRIAGES

BEACH—ELLIOTT.—On Nov. 8, at Leintwardine, Alan Avery William Beach, surgeon lieutenant, R.N.V.R., to Margaret Elliott.

MCOWAN—BACKHOUSE.—On Nov. 1, at Longdon-on-Tern, Salop, Bernard McOwan, surgeon lieutenant, R.N.V.R., to Margaret Clare Backhouse.

WATT—MATTINSON.—On Oct. 28, at Carlisle, George Watt, M.B., to Patricia Mattinson.

DEATHS

BARTON.—On Nov. 4, at Lindisfarne Road, London, S.W., James Kingston Barton, M.R.C.P., aged 87.

BROWN.—On Nov. 6, at Cambridge, Alice Evangeline Brown, M.D. Brux., L.R.C.P.E., of Upper Park Road, Hampstead.

FORDYCE.—On Nov. 6, at Tillicoultry, William Fordyce, M.D. Edin., F.R.C.P.E., F.R.C.O.G., consulting gynæcologist to the Edinburgh Royal Infirmary.

MCCREA.—On Nov. 8, Hugh Moreland McCrea, O.B.E., M.D. R.U.I., of Harley House, London.

MARTIN.—On Nov. 3, John Martin, M.D. Camb., surgeon captain R.N., retd.

MONRO.—On Nov. 3, at Richmond, Surrey, James Donald Rae Monro, M.D. Glasg.

Notes, Comments and Abstracts

THE CASE HISTORY IN DIAGNOSIS

J. PLESCH, M.D. BERLIN, L.R.C.P.E.

DIAGNOSTIC methods employed in medicine have advanced, but insufficient attention has been paid to the importance of the case-history. If we do not discuss his case with the patient we bring medicine to the level of veterinary medicine. In giving a history the patient finds or loses his confidence, and discovers whether he is dealing with merely a man who has studied medicine or with a real doctor. We are led towards a diagnosis by the history of the patient and his illness, by the first impression we get of him and by every fact which our senses are capable of observing; these put us on the right track for deeper exploration of his illness. Diagnosis depends on association of ideas. Neglect of history-taking springs from the rapid development of factual knowledge and of objective methods of examination by physical, chemical, bacteriological and microscopic means. We have lost confidence in our intuitive abilities and do not use or rely on our five senses sufficiently; this is regrettable because medicine must always remain an art to which science is only the servant. In medicine we try to judge the relations of the various functions to each other; it is impossible to reach a diagnosis according to a mechanical scheme. Our judgment must depend partly on imaginative intuition, and we can only pass on to the student the method of making the bricks from which he must build the diagnosis.

Even in many teaching hospitals case-histories consist only of notes on age and sex, diseases of childhood, a few remarks on the family, the symptoms of the onset of the present illness, and a brief account of a superficial examination. Recent work on constitution and heredity and on significant psychological findings is ignored. Usually there is a description of the patient's height, physical development and colouring—in these days of photography. Even the passport office has replaced written descriptions by photographs. Simple photography, coloured photography and the cinematograph can tell more about family likeness, constitution, complexion, temperament and anomalies than any words. They also make it possible to record changes over a period.

History-taking must be accompanied by inspection because the first impression directs investigation. We must also note any constitutional and psychological anomalies. The conditions of the extremities may disclose the duration of the illness: a soft sole of the foot indicates long illness, tough palms hard work; the wrinkles of the face betray whether the temperament is gay, meditative, choleric or depressed; clothing, jewellery, or a tattoo mark all give something away. A small telangiectatic mole in the occipital region, a third nipple like a wart but erectile, hypospadias, cryptorchism, relics of gillclefts, polydactyly and birthmarks all have their psychological projections. Illnesses take a different course in patients with such embryological anomalies. A woman with masculine traits, recognisable by hairs of the pudenda reaching up to the navel, has an entirely different psychical make-up from a woman whose dermatographia shows her extreme femininity. The family history must not be confined to parents and brothers, sisters and children; Mendel's law demands that we should inquire further. It is not so easy to get at the truth about relations, since patients generally dislike disclosing other people's secrets; or the information may be inaccurate because the patient takes a flattering view of his family. Illegitimacy is seldom admitted. It is more difficult still to get at the truth about the patient himself. Exaggeration, understatement, distortion are not always intentional, they often occur because the patient is usually not at all clear about himself; inquiry then becomes a psychoanalytical examination. If we suspect insincerity, or that the patient is trying to disguise the facts, we must get at the truth by clever cross-examination. When the patient becomes aware of his tactical inferiority he will quickly change his attitude and become more confiding. We must, however, make use not only of the facts he tells us but of the lies, for they betray his weaknesses and are sometimes more revealing than the facts themselves.

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A history of previous illness is as a rule difficult to verify. Acidity, liverishness, nervousness, indigestion, rheumatism and similar ambiguous expressions are used freely. Pains are misleadingly related to various organs—backache to the kidneys and sensations in the chest to the heart. The patient must be induced to describe his symptoms and it is pleasing to find how readily even uneducated patients choose the right words, how comprehensibly they describe a cramp, the sudden onset and gradual fading of a colic, the pain of angina pectoris or the distress of an asthmatic attack. By watching the patient closely as he tells his story, by noting his complexion and his gestures, we may find a short cut to the understanding of his trouble. At this stage he tells us what he himself thinks important. It may have little bearing on the essential disease, but we must pay attention to it in order that he may give vent to his feelings. "Les hommes avec le petit papier," described by Charcot, are found not only among the hyperthyroid; we must let them make their points, but circumlocution can be avoided by adroitly placed inquiries for other symptoms.

We must, of course, be cautious in accepting the patient's estimates of size or quantity. The appetite is always measured by comparison with the appetite of those about him, the state of the bowels by the number, not the size, of the actions; sweating is reckoned in changes of nightwear; it is difficult to get any estimate of the daily urine; hæmorrhage will be counted by the size of the vessel in which it is emptied; sputum is always a cupful; menstruation is estimated by the number of changed towels.

Few events are more significant in physical and psychical development than adolescence. The less disturbance there is during this transitional phase the more likely is the later sexual life to be normal, and vice versa. An otherwise incomprehensible illness may be explained by hormonal imbalance in those whose adolescence was disturbed. Delicacy and skill are needed to get truthful information about the sexual life, but a full inquiry will often evoke surprisingly rapid improvement in neurotic cases.

Have we perhaps overrated the value of objective methods of examination? Examination of organs or systems will enable us to localise the change in them, but it is merely a form of diagnostic sport to be able to assert that somebody died from cirrhosis of the liver, from pulmonary tuberculosis or from valvular disease. What we ought to find out is how it was possible for the patient to go on living at all before his cirrhosis, his tuberculosis or his incompetent valves killed him. This will teach us what adjustments the body makes to its diseased organs, and may point the way to compensatory treatment. We are turning nowadays from the study of dead pathology to that of living function, from the organs to the organism.

Physiology is only concerned with conditions in the normal body, and experiments often deal with such extreme states as starvation or of utter repletion—of intense activity of functions or of almost complete arrest. Experiments on organs and tissues in vitro are still too often taken to represent the actual processes in vivo. Such investigations cannot mimic the coördinated, automatic and compensatory mechanisms which operate in the living organism; they are only the separate stones in the mosaic. They do not show what made life possible when an organ was grossly damaged. Restitutio ad integrum is a rare thing in pathology; our treatment must aim at supporting the body's natural compensating mechanisms.

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Collectively men can be regarded as statistics, but in practice the doctor must know the idiosyncrasies of each patient so that, for example, he can tell whether in an epidemic of typhoid that patient will be one of the 15% of fatal cases or not. In the relationship between the individual and the disease it is the individual who varies. For instance, two cases of stomach ulcer of similar size and location will not, as a rule, justify the same prognosis or treatment. A full case-history may indicate how and why the patient fell ill, or incurred an accident. There

may be some incipient nervous disorder which delayed reaction time, or impaired coördination, or accident may be coupled with early signs of tabes or cerebral tumour, syringomyelia, arteriosclerosis, arthritis, or ocular or aural diseases. The case-history may throw light on such integrative functions as complexion, respiration, pulse, appetite, sweating, temperature, sleep, posture, gait, and weight.

The best way to assess the state of a function is to suggest to the patient an exercise which calls on that function and to watch his reaction to the suggestion. Thus one asks a man with cardiac insufficiency (even though he shows hardly any sign of it when at rest) whether he could run up five flights of stairs—the look of astonishment on his face will indicate plainly enough the presence of cardiac damage. The mere thought of the effort makes him profoundly anxious. The information derived from a test-meal is meagre compared to that which we may gather by talking to the patient about his favourite dishes. Offered a glass of melted butter, a man with high gastric acidity would accept it, whereas a man with hypo-acidity would register disgust at the mere thought. The psychophysical reflex is so graded that one might almost speak of "psychological titration" of the stomach juice.

But we must realise that our relation to the patient is reciprocal; we analyse him by his answers, he analyses us by our questions. It is this psychoanalysis of the psychoanalyst which creates mutual confidence and, alas, also disappointments. The task of history-taking is too important to be left to the younger members of the staff. A broad view, readiness to understand and sympathise, kindliness, ability to judge without severity, to encourage, instruct, advise and attract—all these are needed in the taking of a case-history, and in no phase of medical activity are experience and knowledge more necessary.

POLISH FACULTY OF MEDICINE AT EDINBURGH UNIVERSITY

AT the Royal Society of Medicine on Nov. 5 Prof. A. T. Jurasz, dean of the Polish Faculty of Medicine within the University of Edinburgh, addressed the history section on the foundation and achievements of the faculty. He described the events which led up to the creation of this university within a university. The occupation of Poland lost the Poles their academic institutions, research centres and libraries, and exterminated the cultural life of Poland as a whole. The Polish Medical Faculty was to a certain extent symbolic of the need for all countries to maintain the standards of Western culture in the face of the destructive power of Nazi Germany. The faculty was formed by the unanimous resolution of the Medical Faculty of Edinburgh, followed by the acceptance of the scheme by the senate; the inaugural ceremony, in the presence of the President of the Polish Republic, took place on March 22, 1941. The first academic year was rather concentrated because there were no holidays. It was carried through without a break, and the second year has now started. The enrolments in the first year were 77 and in the second year 120 students. The first person to graduate was a Polish officer-pilot in the R.A.F.; he took part in many flights over Germany, but nevertheless found time to prepare for his final examination. During the last academic year 640 hours of lectures were given for the first-year students, and 1160 hours for the fourth and fifth years. The laboratories, the lecture-theatres and the wards of the various institutions of the university are open to the Poles. Professor Jurasz suggested that something more than mere chance had determined that Edinburgh should become the seat of the faculty. There were old cultural links between the two countries. In the 18th and 19th centuries Scots came to Poland. Later Edinburgh University became a cultural centre for many prominent Poles, and they used the experience gained in Scotland in founding clinics and scientific institutions in Poland, and even in reforming the teaching of medical science in the University of Cracow. The foundation of the faculty was symbolic of the collaboration which would exist after the war.

Dr. J. F. Halls Dally, president of the section, pointed out that however much help had been given by others, Professor Jurasz was essentially responsible for the success of the enterprise. Dr. E. Ashworth Underwood suggested that after the war it might be possible to establish a small British faculty of medicine in various continental universities, thus permitting certain students to finish their studies abroad—and acquire a practical knowledge of the language and culture of the people among whom they resided. Sir Alfred Webb-Johnson expressed his great interest in the unique Edinburgh experiment, and Dr. W. Clarke Trotter discussed the historic relations between Poland and the University of Edinburgh.

The address was preceded by a small luncheon in honour of Professor Jurasz, and after the meeting a reception was given by the Polish Ambassador at the Embassy.

FAREWELL, CHOCOLATE SOLDIER

THE American Army has exchanged the chocolate ration of the soldier in the field for five pieces of hard candy, individually wrapped and in assorted flavours (*J. Amer. med. Ass.* 1941, **117**, 941). Recent fatigue tests at Minnesota University have shown that men have a greater energy output if they take sugar periodically through the day rather than in large quantities at mealtimes.

Sugar for the Services,
Candy for the troops—
A soldier shorn of sugar
Invariably droops.

If you want your soldiers
Stiffened at the waist
Give them sugar candy,
Flavouring to taste.

Forget Papa's instructions,
Forget Mamma's appeals—
The energetic soldier
Must eat between his meals.

MIDDLE INCOMES AT BRISTOL

THEIR honorary staffs have lately asked the Bristol voluntary hospitals if they will in future rigidly observe the B.M.A. scale. This means that except in emergencies nobody above the following income-limits will be admitted to the general wards or outpatient departments of the hospitals:

£312 married with dependants
£260 married without children.
£208 single without depefidants.

The Bristol Hospitals Fund recognises the doctors' right to fix the line of income-demarcation above which they cannot afford to treat patients for nothing, and it also recognises the difficulties of those with incomes just above the scale, who can afford to pay for most of their medical treatment but cannot find the fees of specialist and surgeon. Anticipating the Nuffield provident scheme the fund has devised what it calls an intermediate contributory scheme. The name is dictated by ambition, for it is hoped soon to start yet another scheme for those with still larger incomes. The intermediate scheme was launched by Mr. Egbert Cadbury at a meeting of the fund last July. The fund has made an arrangement with the Bristol voluntary hospitals, by which intermediate members for the payment of 6*d*. a week can provide for consultation, operations and treatment for themselves and their dependants. People within the following income limits are eligible:

£416 married with dependants
£364 married without children
£260 single without dependants.

The only exception to this arrangement is the Bristol Eye Hospital, and even here a modified scale of fees has been arranged for members of the scheme. The scheme can only be operated through the fund.

The fund, as a contributory scheme, has no legal power to make grants to medical staffs, and the board of each hospital is therefore recommended to make a grant to their medical staff fund equivalent to a third of the amount they receive from the fund for treating the intermediate contributory scheme patients. The staff will also receive a quarter of any surplus that may accrue.

ORIGINAL ARTICLES

THE COMMON SULPHONAMIDES
NOMENCLATURE, STRUCTURE AND USES

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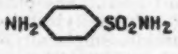
WITH the inevitable increase in the number of compounds introduced into clinical practice for the chemotherapy of bacterial infections the need of an accurate and uniform nomenclature becomes urgent. Few modern British books on general medicine or the specialties make any attempt to achieve accuracy in the names used for these compounds, and the medical journals and encyclopædias tend to pander to the whims of their contributors instead of exerting strict control over the names employed. As a consequence, for example, all the names which happen to have been employed for the same chemical compound by various contributors to a textbook may appear in different parts of the index. Abstracts of articles from foreign journals often use for drugs names which are unfamiliar to readers in this country and in this way the chief point of the abstract may be lost. Conversely, proprietary names and erroneous nomenclature in English articles duly find their way into foreign abstracts to the mystification of readers. The practitioner who writes a prescription for "sulphonamide," ½ gramme tablets, or the surgeon who orders a wound to be dressed with sulphonamide powder, does not realise that what he has ordered is meaningless. The writer of an article who describes the treatment of a patient with "Prontosil" given by mouth in such and such a dosage overlooks the fact that there are three distinct chemical compounds to which this name is applied, and that all are given by mouth. The limit appears to have been reached by the author of an article on the use of various sulphonamide compounds who calmly announced at the outset that a particular brand name for sulphanilamide would be used to describe all the different compounds employed! It therefore seems opportune to suggest a few rules for general guidance. First, about dosage. The common practice of describing oral dosage in terms of number of tablets or volume of a suspension is inadvisable. A discussion once arose concerning an article on the treatment of gonorrhœa in which the dosage of sulphanilamide employed was in dispute until it was realised that the author was expressing dosage in drachms of a proprietary suspension. Dosage should always be expressed in terms of the active ingredient.

Most of the sulphonamides in common use have three kinds of name—a chemical name often occupying a line of print, a scientific synonym or pet-name, being the chemical name in a shortened form, and a various number of trade names. The synonym is the one intended for use in scientific articles, but unfortunately not all the compounds have one, and in some cases the trade name is at present unavoidable. Whenever possible only the full chemical name or its shortened form should be used, though it may sometimes be convenient to indicate once in an article which particular brand was employed.

SULPHANILAMIDE AND ITS EARLIER DERIVATIVES

Para-aminobenzenesulphonamide or para-aminophenylsulphonamide is the simplest and most widely used of these drugs, and being the amide of sulphanilic acid the name now commonly adopted of sulphanilamide is at once both accurate and brief, and the employment of proprietary names for this compound in medical literature is inexcusable. Of the forty or so trade names indicating proprietary brands of this compound the commonest ones in this country are Colsulanyde, Prontosil album and Streptocide, and sometimes the non-proprietary designations sulphonamide-P or P.A.B.S. are used. A proprietary brand much used in America is known as Prontylin. Some clinicians still do not realise that these names all stand for the same substance, and it is not unusual to hear of a patient's treatment being changed from one make of sulphanilamide to another, because he did not respond to the brand first ordered. Many other proprietary names for sulphanilamide, less commonly used than the four already given, are encountered, chiefly in foreign medical literature. In table I will be found 42 trade names for sulphanilamide, among which collectors may find choice and rare specimens. In the case of a few trade names encountered in foreign medical journals there has been no clue to the composition of the drug, or the composition has been variously described in different articles so that it has been impossible to be certain what the compound was. Sulphanilamide was included in the Fourth Addendum to the B.P. 1932.



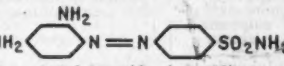
Sulphanilamide

TABLE I—PROPRIETARY NAMES FOR SULPHANILAMIDE

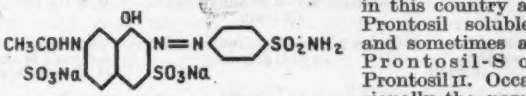
Albosal	Gombardol	Septamide album	Streptocom
Ambesid	Lysococcine	Septanilam	Strepton
Antistrept	Neococcyl	Septinal	Streptozone
Astreptine	Orgaseptine	Septoplix	Sulfamidyl
Bacteramide	Prontosil album	Stopton album	Sulfana
Bactesid	Prontylin	Stramid	Sulfanil
Cepticide	Pronzin album	Strepamide	Sulphanalone
Colsulanyde	Proseptine	Streptamid	Supron
Desceptyl	Proseptol	Streptazol	Therapol
Ergaseptine	Pysoccine	Streptocide	
Erysipan	Rubiazol-A	Streptoclase	

The simplest and most convenient classification of other sulphonamide drugs is to regard them as derivatives of sulphanilamide and as falling into two groups according to whether substitution takes place in the amino (NH_2) or in the amide (SO_2NH_2) portion of the molecule (table II). All the earlier compounds belong to the first class and are split up with release of sulphanilamide in the body. The more active substances introduced subsequently, such as sulphapyridine and sulphathiazole, fall into the second category, and these compounds do not depend for their action on the production of sulphanilamide.

The first compound to be employed was sulphonamido-chrysoïdin, which is 4′-sulphonamido-2 : 4-diaminoazobenzene, introduced into commerce under the name prontosil after having been called Streptozon. The name prontosil strictly refers, therefore, to this azo dye-stuff but most English clinicians use it to designate sulphanilamide. If the word is used at all it should never be employed without qualification, so that there is no doubt as to meaning. Sulphonamido-crysoïdin is also known as Prontosil flavum or Prontosil rubrum. A less common trade name is Pronzin rubrum. A more soluble compound was later introduced for parenteral administration, which consists of a solution of the disodium salt of 4′-sulphonamidobenzene-2-azo-1-hydroxy-7-acetylaminonaphthalene-3 : 6-disulphonic acid, usually known in this country as Prontosil soluble, and sometimes as Prontosil-S or Prontosil II. Occasionally the name prontosil is applied to this compound instead of to sulphonamido-chrysoïdin, and in America, where it is given by mouth in place of the latter, it is known under the proprietary name of Neoprontosil, the "descriptive non-proprietary name" proposed for this substance by the Council on Pharmacy and Chemistry of the American Medical Association being azosulfamide. The name streptozon has been given to both prontosil rubrum and prontosil soluble, the latter having sometimes been distinguished as Streptozon II or S, and curiously enough the designation Prontosil red is sometimes used for prontosil soluble rather than prontosil rubrum. The Rubiazols include the French equivalents of the German azo sulphonamides and rival them in confused terminology. It is, however, sufficient to remember that in this country the name rubiazol is applied to a compound which differs from sulphonamido-chrysoïdin in containing a carboxyl (COOH) grouping, and hence is conveniently described as carboxysulphonamido-chrysoïdin.



Sulphonamido-chrysoïdin



Azosulphamide (Prontosil soluble)

In common with most other compounds of the first group in which substitution takes place in the amino